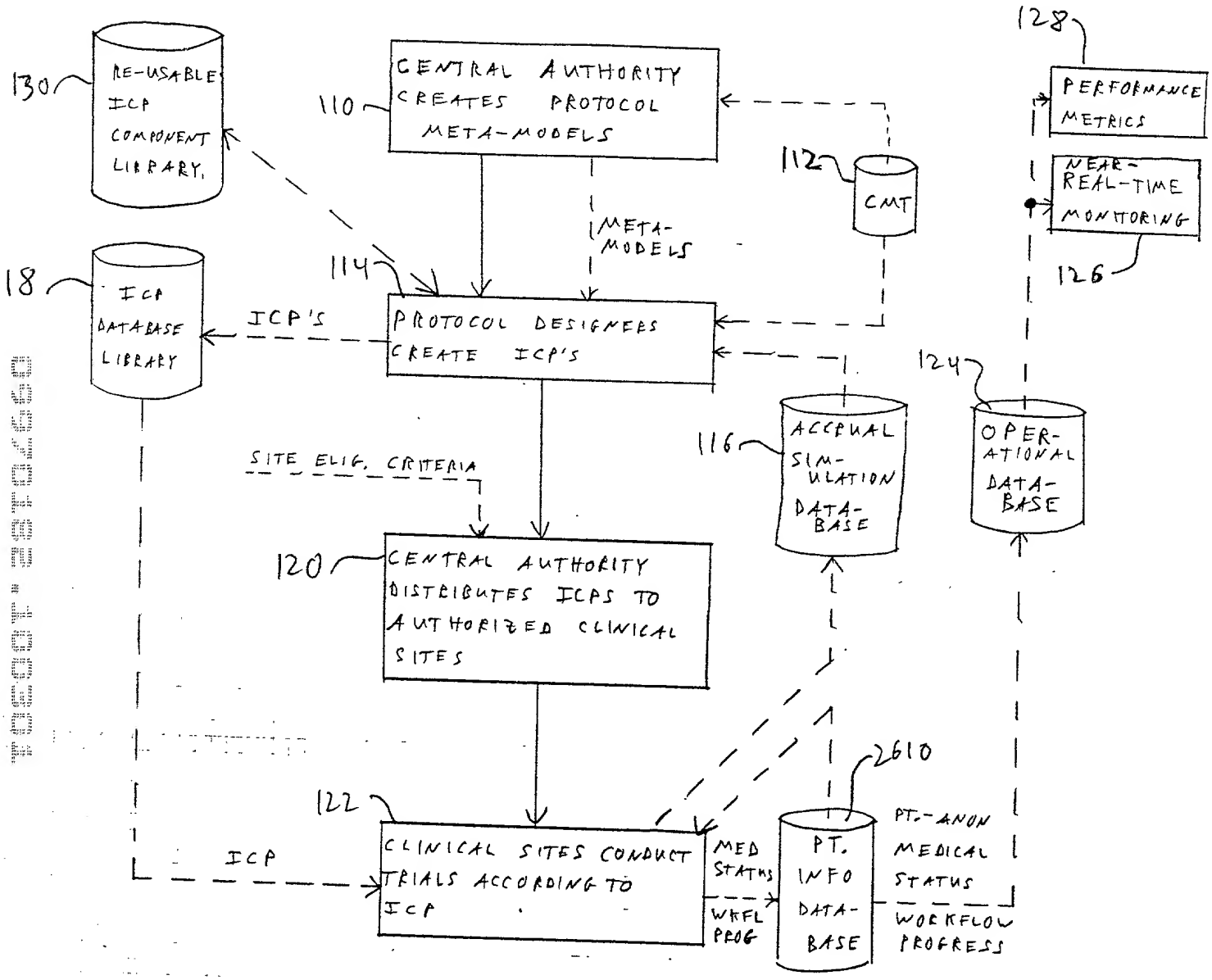

130
RE-USABLE ICP COMPONENT LIBRARY
110
CENTRAL AUTHORITY CREATES PROTOCOL META-MODELS
META-MODELS
112
CMT
128
PERFORMANCE METRICS
NEAR-REAL-TIME MONITORING
126
118
ICP DATABASE LIBRARY
ICP'S
114
PROTOCOL DESIGNERS CREATE ICP'S
124
116
ACCRUAL SIM-ULATION DATA-BASE
OPER-ATIONAL DATA-BASE
SITE ELIG. CRITERIA
120
CENTRAL AUTHORITY DISTRIBUTES ICPS TO AUTHORIZED CLINICAL SITES
2610
122
ICP
CLINICAL SITES CONDUCT TRIALS ACCORDING TO ICP
MED STATUS
WRFL PROG
PT. INFO DATA-BASE
PT.-ANON MEDICAL STATUS
WORKFLOW PROGRESS

Fig. 1

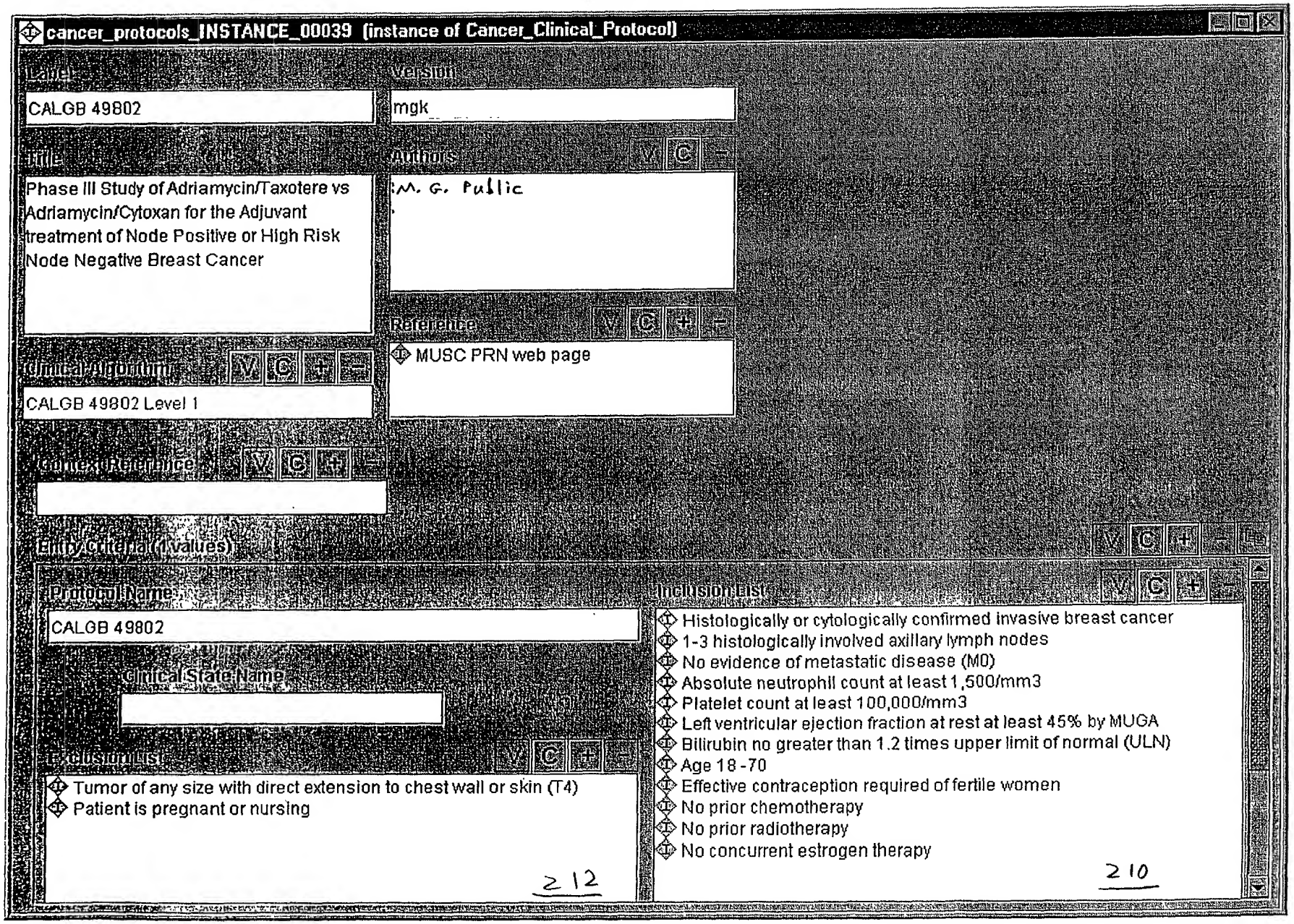

cancer_protocols_INSTANCE_00039 (instance of Cancer_Clinical_Protocol)
Label
CALGB 49802
Version
mgk
Title
Phase III Study of Adriamycin/Taxotere vs Adriamycin/Cytoxan for the Adjuvant treatment of Node Positive or High Risk Node Negative Breast Cancer
Authors
M. G. Public
Reference
MUSC PRN web page
Clinical Algorithm
CALGB 49802 Level 1
Context Reference
Entry Criteria (1 values)
Protocol Name
CALGB 49802
Clinical State Name
Exclusion List
Tumor of any size with direct extension to chest wall or skin (T4)
Patient is pregnant or nursing
212
Inclusion List
Histologically or cytologically confirmed invasive breast cancer
1-3 histologically involved axillary lymph nodes
No evidence of metastatic disease (M0)
Absolute neutrophil count at least 1,500/mm3
Platelet count at least 100,000/mm3
Left ventricular ejection fraction at rest at least 45% by MUGA
Bilirubin no greater than 1.2 times upper limit of normal (ULN)
Age 18-70
Effective contraception required of fertile women
No prior chemotherapy
No prior radiotherapy
No concurrent estrogen therapy
210

Fig. 2

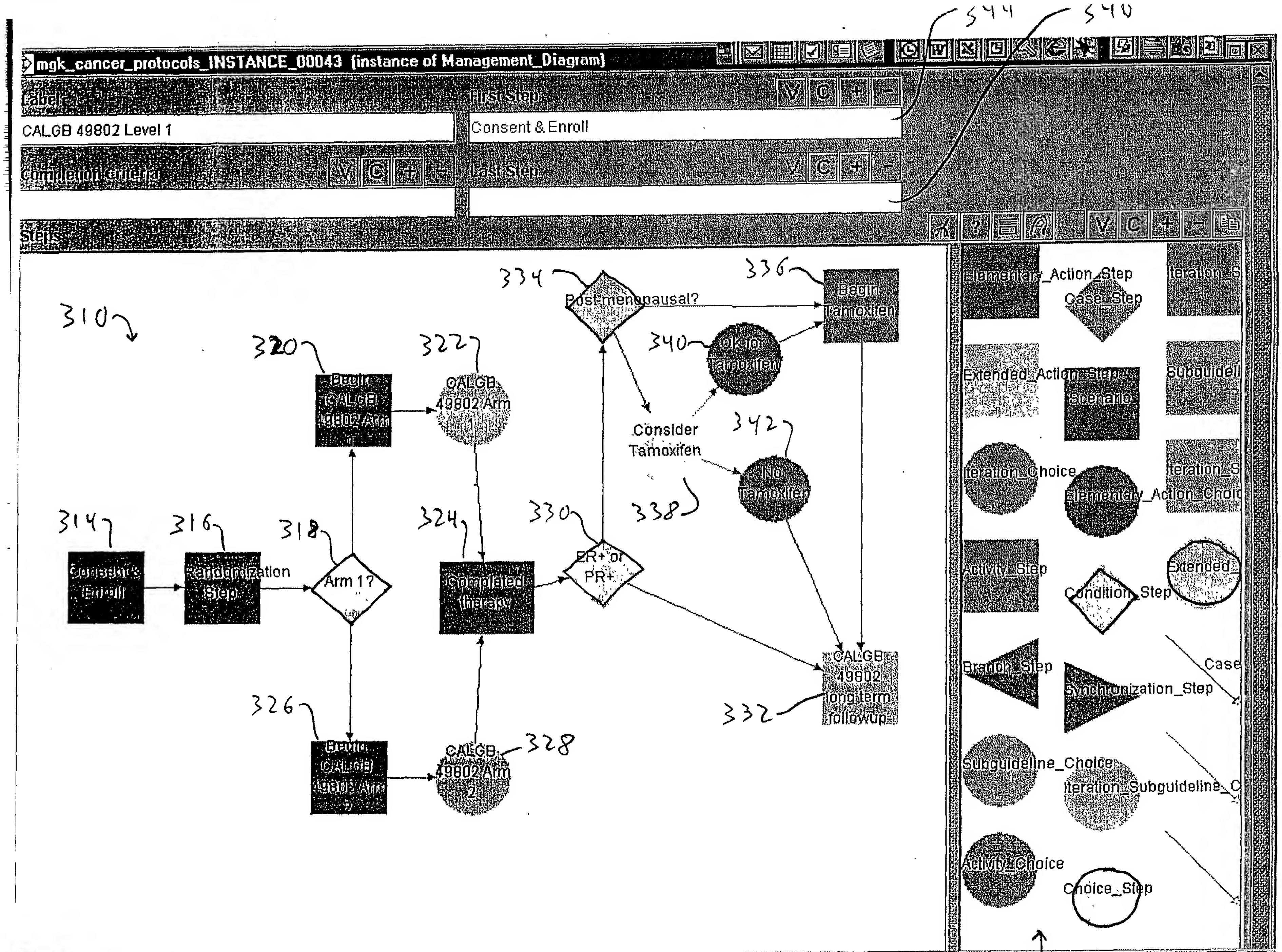

mgk_cancer_protocols_INSTANCE_00043 (instance of Management_Diagram)
Label
CALGB 49802 Level 1
First Step
Consent & Enroll
Completion criteria
Last Step
Steps
310
312
314
316
318
320
322
324
326
328
330
332
334
336
338
340
342
344
346
Consent & Enroll
Randomization Step
Arm 1?
Begin CALGB 49802 Arm 1
Begin CALGB 49802 Arm 2
CALGB 49802 Arm 1
CALGB 49802 Arm 2
Completed therapy
ER+ or PR+
Post-menopausal?
Consider Tamoxifen
OK for Tamoxifen
No Tamoxifen
Begin Tamoxifen
CALGB 49802 long term followup
Elementary_Action_Step
Case_Step
Extended_Action_Step
Scenario
Iteration_Choice
Elementary_Action_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Subguideline_Choice
Iteration_Subguideline_C
Activity_Choice
Choice_Step
Case

Fig. 3

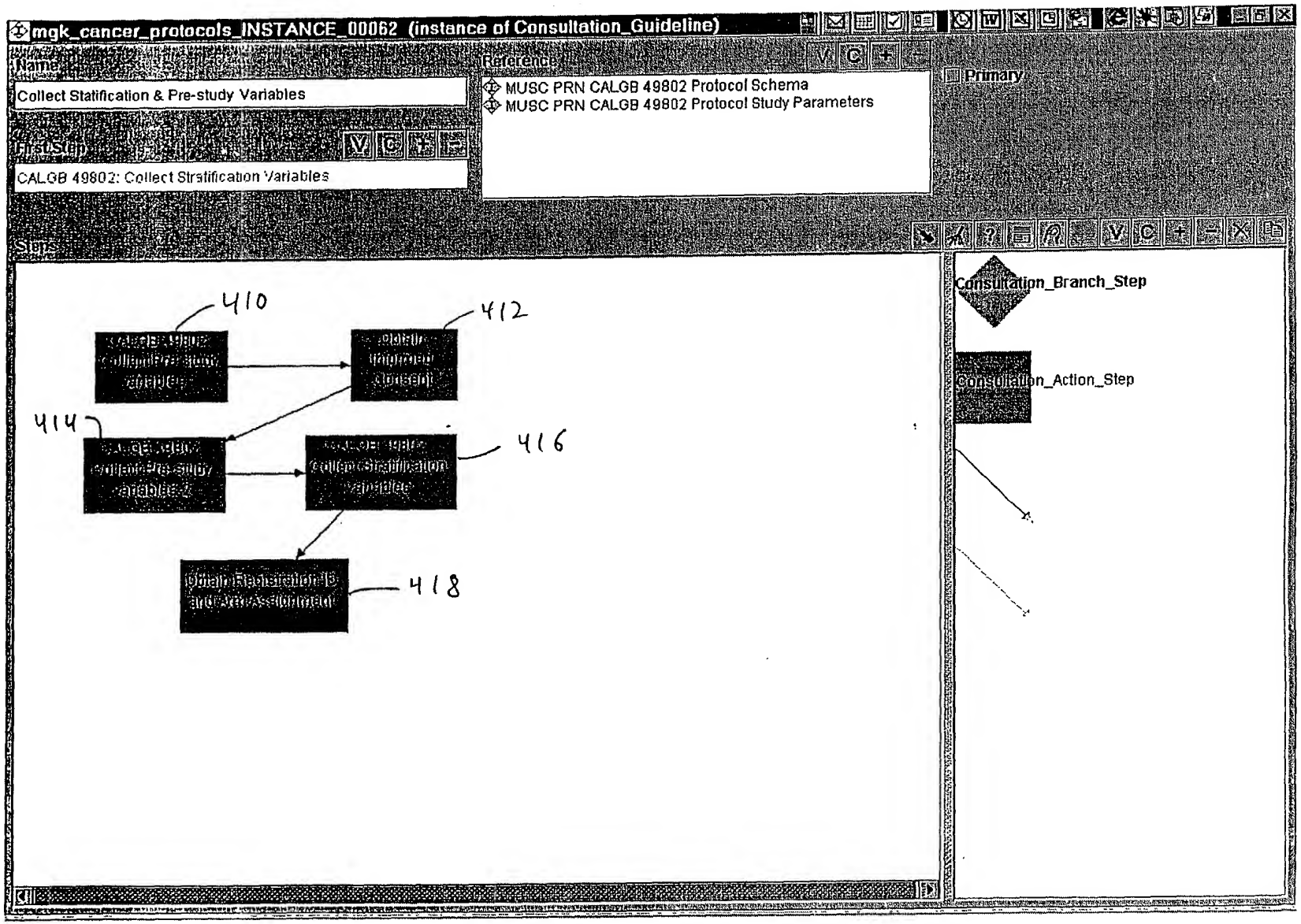


Fig. 4

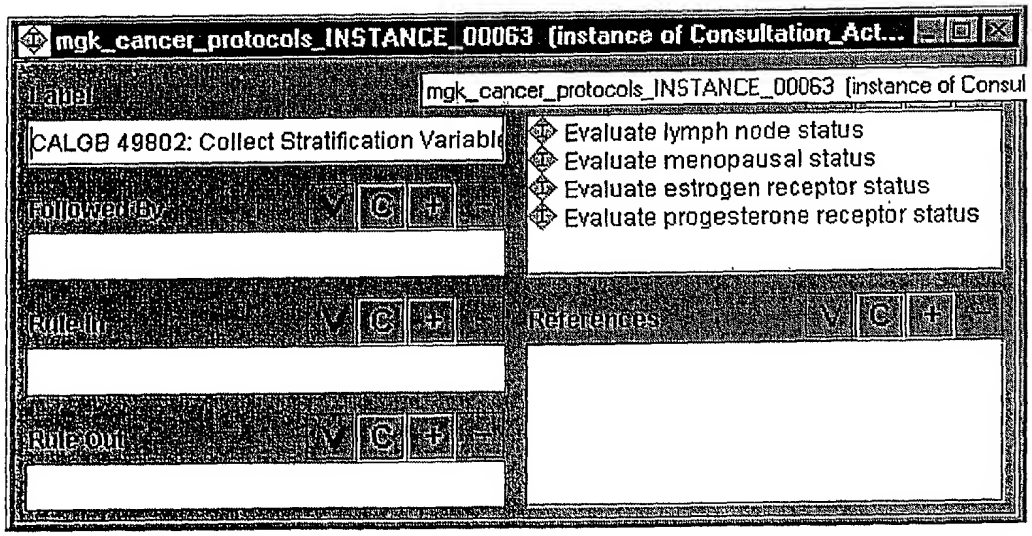


Fig. 5

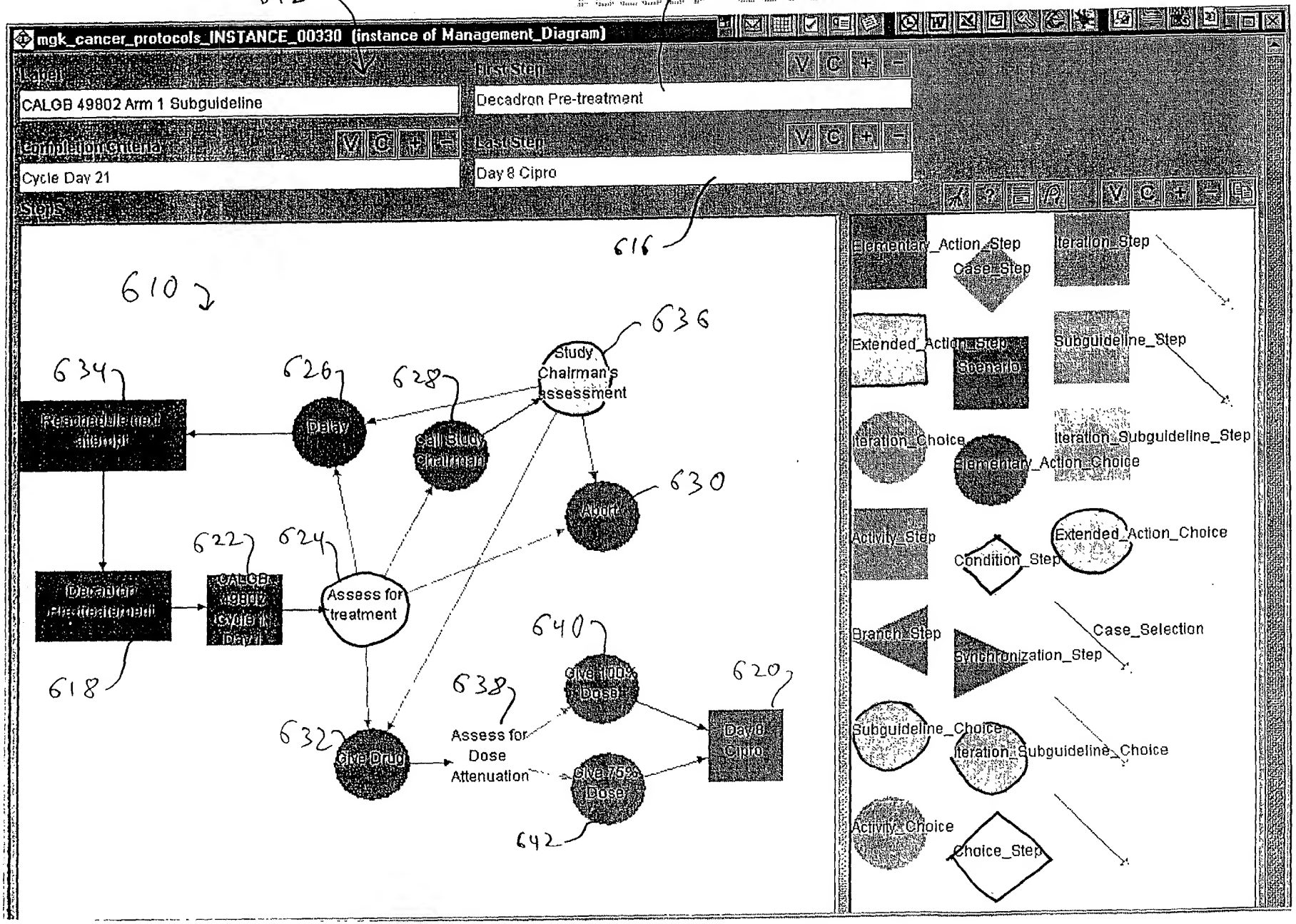

612
614
mgk_cancer_protocols_INSTANCE_00330 (instance of Management_Diagram)
Label
CALGB 49802 Arm 1 Subguideline
First Step
Decadron Pre-treatment
Completion Criteria
Cycle Day 21
Last Step
Day 8 Cipro
Steps
616
610
634
636
626
628
Study Chairman's assessment
Delay
Call Study Chairman
630
Abort
622
624
Assess for treatment
618
640
Give 100% Dose
638
620
Assess for Dose Attenuation
632
Give Drug
Give 75% Dose
642
Day 8 Cipro
Elementary_Action_Step
Case_Step
Iteration_Step
Extended_Action_Step
Scenario
Subguideline_Step
Iteration_Choice
Elementary_Action_Choice
Iteration_Subguideline_Step
Activity_Step
Condition_Step
Extended_Action_Choice
Branch_Step
Synchronization_Step
Case_Selection
Subguideline_Choice
Iteration_Subguideline_Choice
Activity_Choice
Choice_Step

Fig. 6

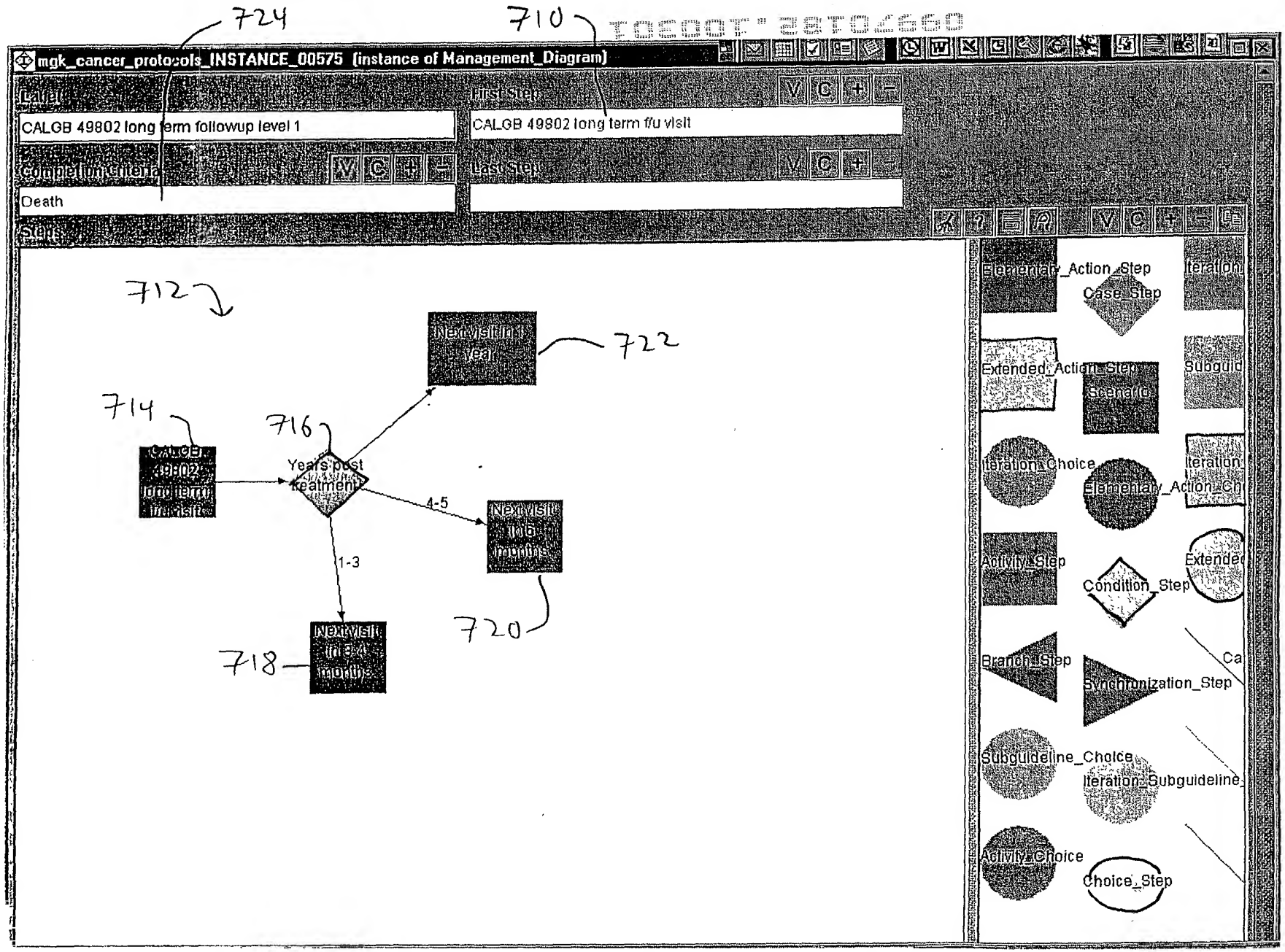

724
710
mgk_cancer_protocols_INSTANCE_00575 (instance of Management_Diagram)
Label
CALGB 49802 long term followup level 1
First Step
CALGB 49802 long term f/u visit
Completion Criteria
Death
Last Step
Steps
712
Next visit in 1 year
722
714
716
Years post treatment
4-5
1-3
Next visit in 6 months
720
718
Next visit in 3-4 months
Elementary_Action_Step
Case_Step
Iteration
Extended_Action_Step
Scenario
Subguid
Iteration_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Subguideline_Choice
Iteration_Subguideline
Activity_Choice
Choice_Step

Fig. 7

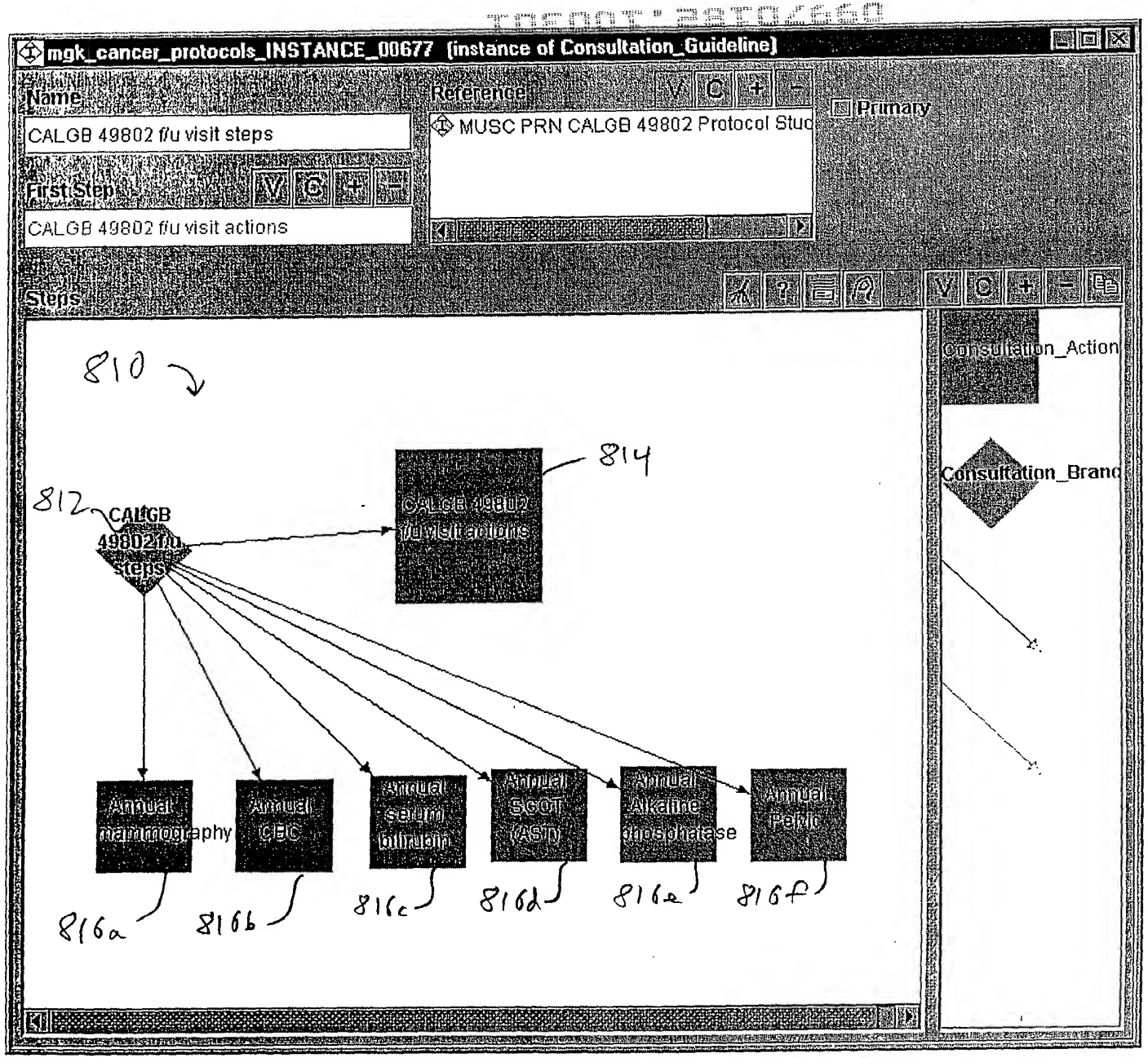

mgk_cancer_protocols_INSTANCE_00677 (instance of Consultation_Guideline)
Name
CALGB 49802 f/u visit steps
Reference
MUSC PRN CALGB 49802 Protocol Stud
Primary
First Step
CALGB 49802 f/u visit actions
Steps
Consultation_Action
Consultation_Brand
810
812
CALGB 49802 f/u steps
814
CALGB 49802 f/u visit actions
Annual mammography
Annual CBC
Annual serum bilirubin
Annual SGOT (AST)
Annual Alkaline phosphatase
Annual Pelvic
816a
816b
816c
816d
816e
816f

Fig. 8

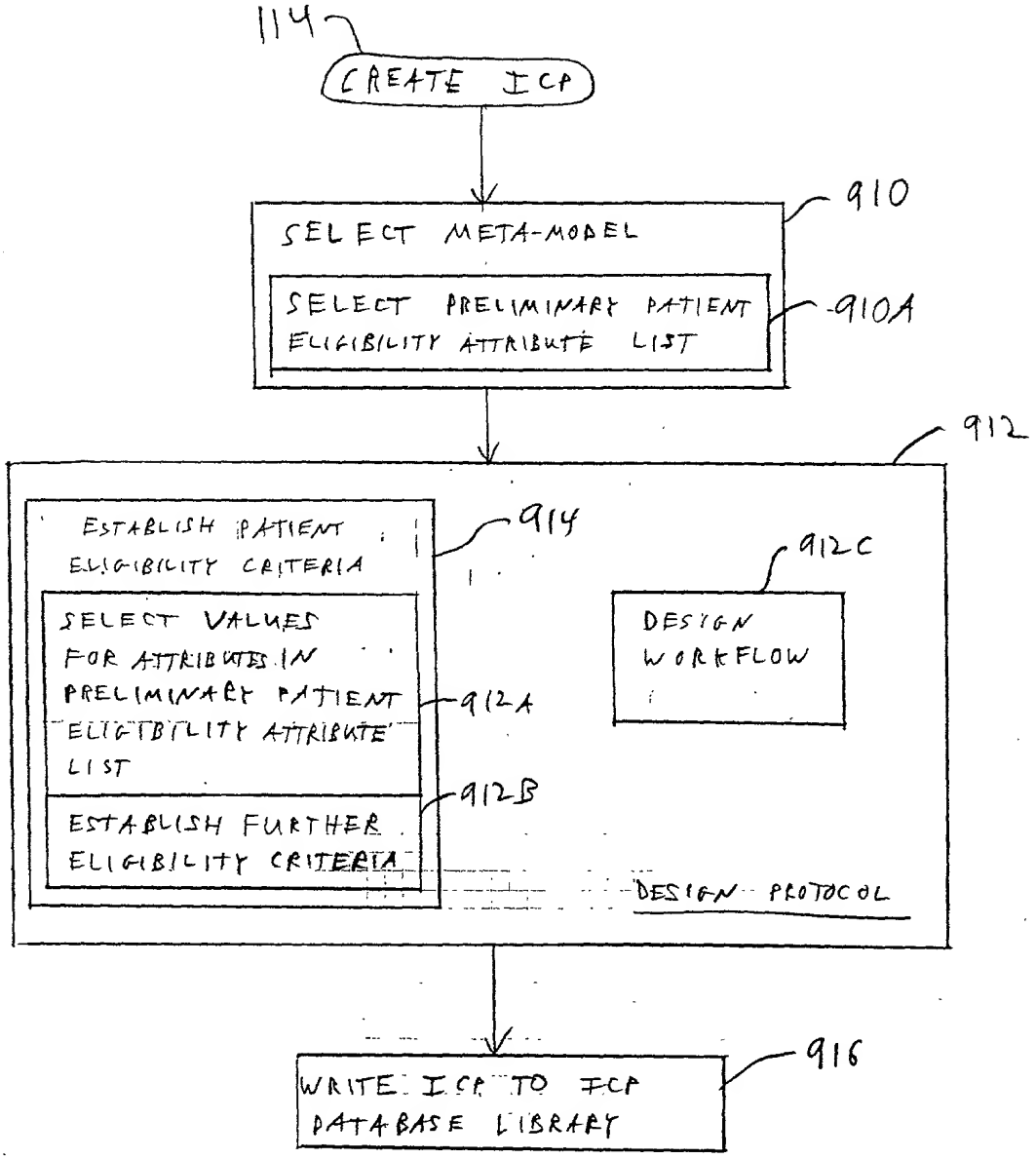

114
CREATE ICP
910
SELECT META-MODEL
SELECT PRELIMINARY PATIENT ELIGIBILITY ATTRIBUTE LIST
910A
912
ESTABLISH PATIENT ELIGIBILITY CRITERIA
914
912C
DESIGN WORKFLOW
SELECT VALUES FOR ATTRIBUTES IN PRELIMINARY PATIENT ELIGIBILITY ATTRIBUTE LIST
912A
912B
ESTABLISH FURTHER ELIGIBILITY CRITERIA
DESIGN PROTOCOL
916
WRITE ICP TO ICP DATABASE LIBRARY

Fig. 9

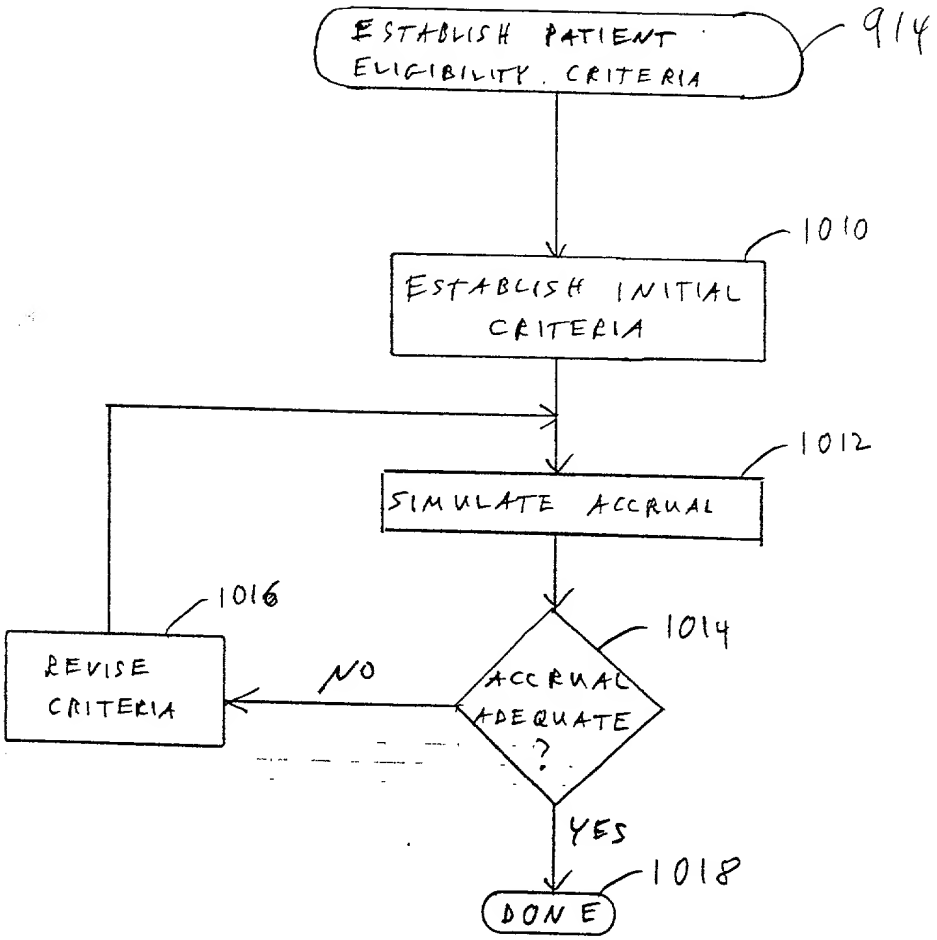

ESTABLISH PATIENT ELIGIBILITY CRITERIA
914
ESTABLISH INITIAL CRITERIA
1010
SIMULATE ACCRUAL
1012
ACCRUAL ADEQUATE ?
1014
NO
REVISE CRITERIA
1016
YES
DONE
1018

Fig. 10

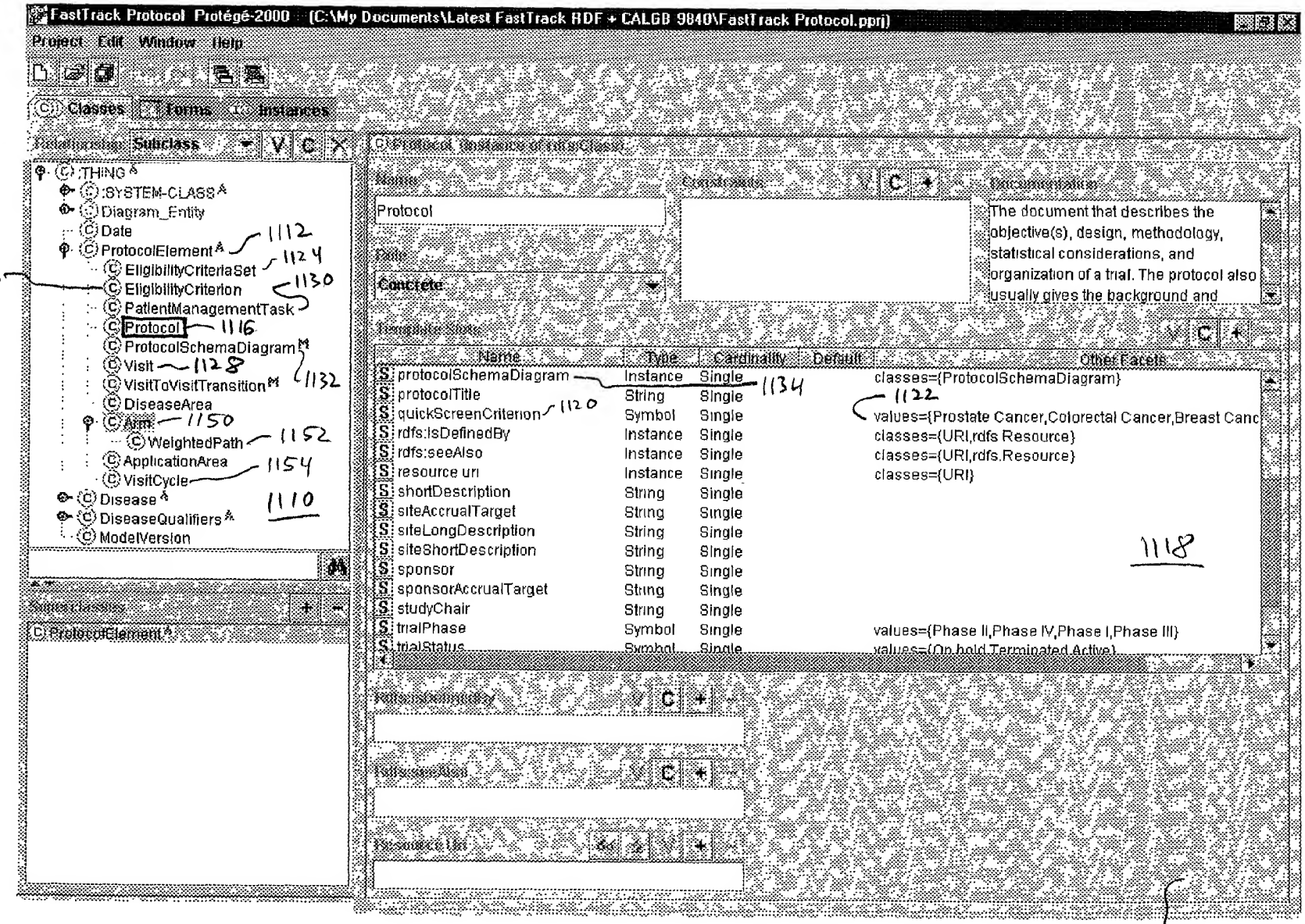

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Subclass
THING
:SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease
DiseaseQualifiers
ModelVersion
ProtocolElement
Name
Protocol
Concrete
The document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol also usually gives the background and
Name Type Cardinality Default Other Facets
protocolSchemaDiagram Instance Single classes={ProtocolSchemaDiagram}
protocolTitle String Single
quickScreenCriterion Symbol Single values={Prostate Cancer,Colorectal Cancer,Breast Canc
rdfs:isDefinedBy Instance Single classes={URI,rdfs Resource}
rdfs:seeAlso Instance Single classes={URI,rdfs.Resource}
resource uri Instance Single classes={URI}
shortDescription String Single
siteAccrualTarget String Single
siteLongDescription String Single
siteShortDescription String Single
sponsor String Single
sponsorAccrualTarget String Single
studyChair String Single
trialPhase Symbol Single values={Phase II,Phase IV,Phase I,Phase III}
trialStatus Symbol Single values={On hold,Terminated,Active}
1126
1112
1124
1130
1116
1128
1132
1150
1152
1154
1110
1134
1122
1120
1118
1114

Fig. 11

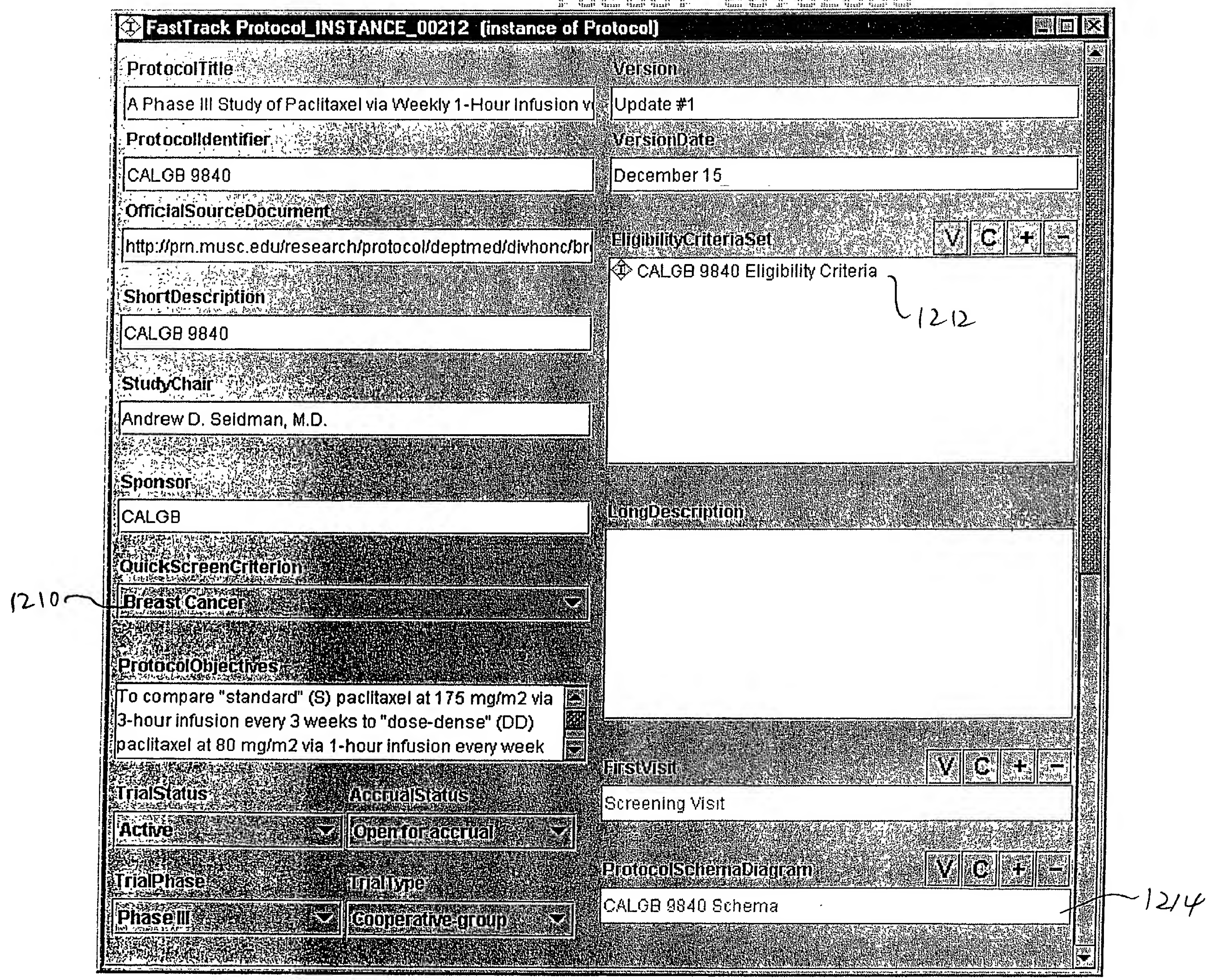

FastTrack Protocol_INSTANCE_00212 (instance of Protocol)
ProtocolTitle
A Phase III Study of Paclitaxel via Weekly 1-Hour Infusion v
Version
Update #1
ProtocolIdentifier
CALGB 9840
VersionDate
December 15
OfficialSourceDocument
http://prn.musc.edu/research/protocol/deptmed/divhonc/br
EligibilityCriteriaSet
V
C
+
-
CALGB 9840 Eligibility Criteria
1212
ShortDescription
CALGB 9840
StudyChair
Andrew D. Seidman, M.D.
Sponsor
CALGB
LongDescription
QuickScreenCriterion
1210
Breast Cancer
ProtocolObjectives
To compare "standard" (S) paclitaxel at 175 mg/m2 via 3-hour infusion every 3 weeks to "dose-dense" (DD) paclitaxel at 80 mg/m2 via 1-hour infusion every week
FirstVisit
Screening Visit
TrialStatus
Active
AccrualStatus
Open for accrual
TrialPhase
Phase III
TrialType
Cooperative group
ProtocolSchemaDiagram
CALGB 9840 Schema
1214

Fig. 12

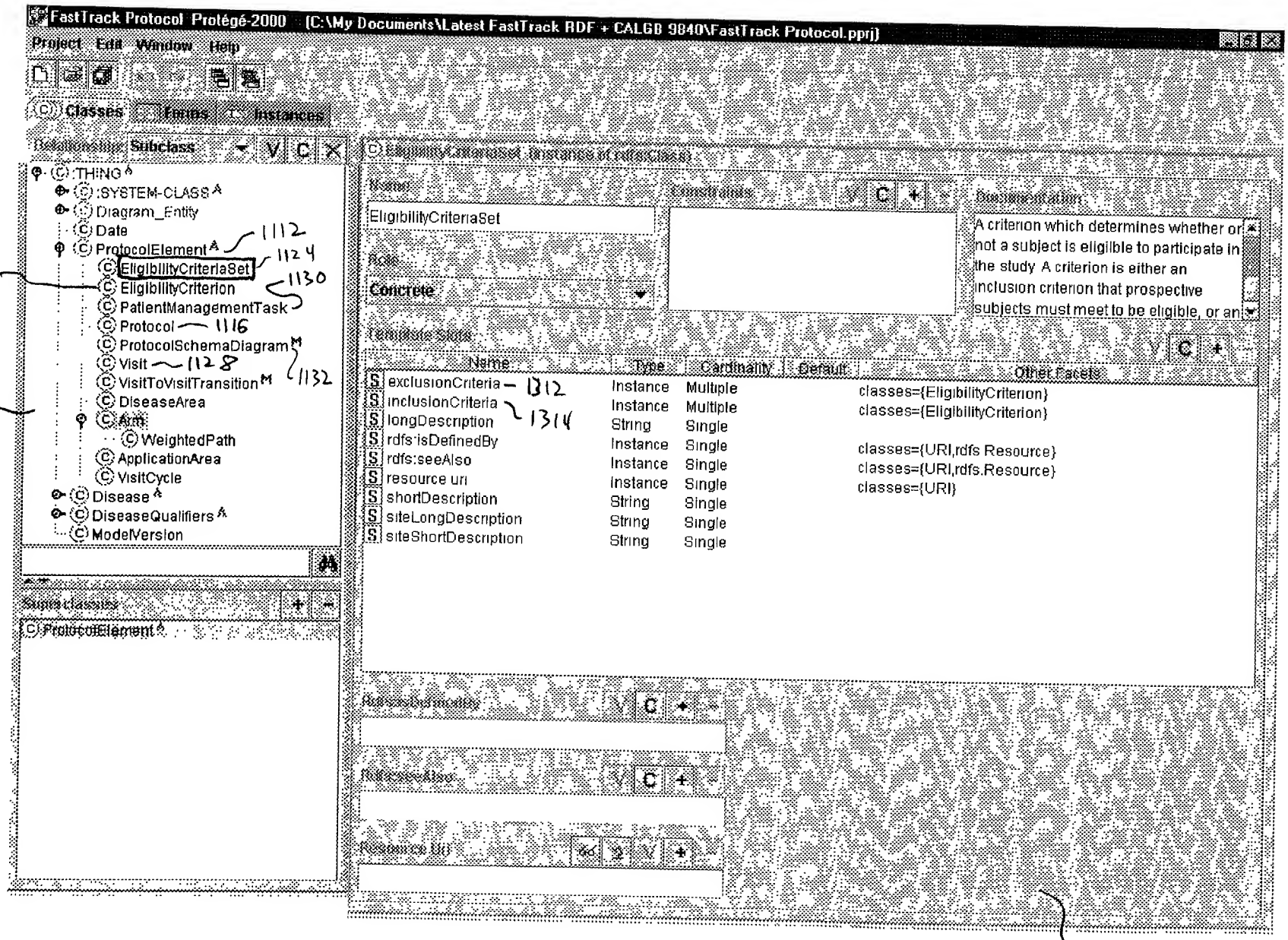


Fig. 13

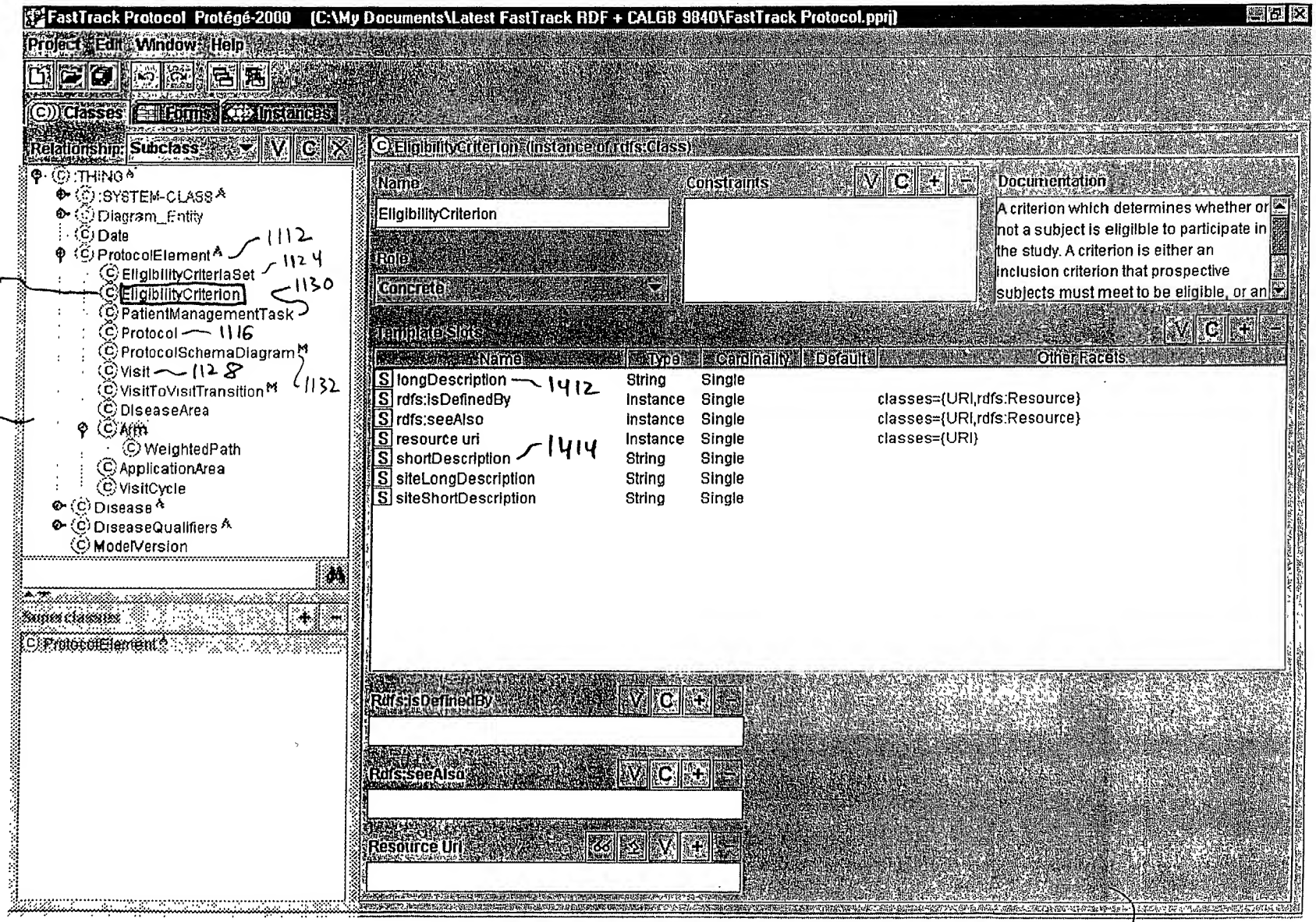


Fig. 14

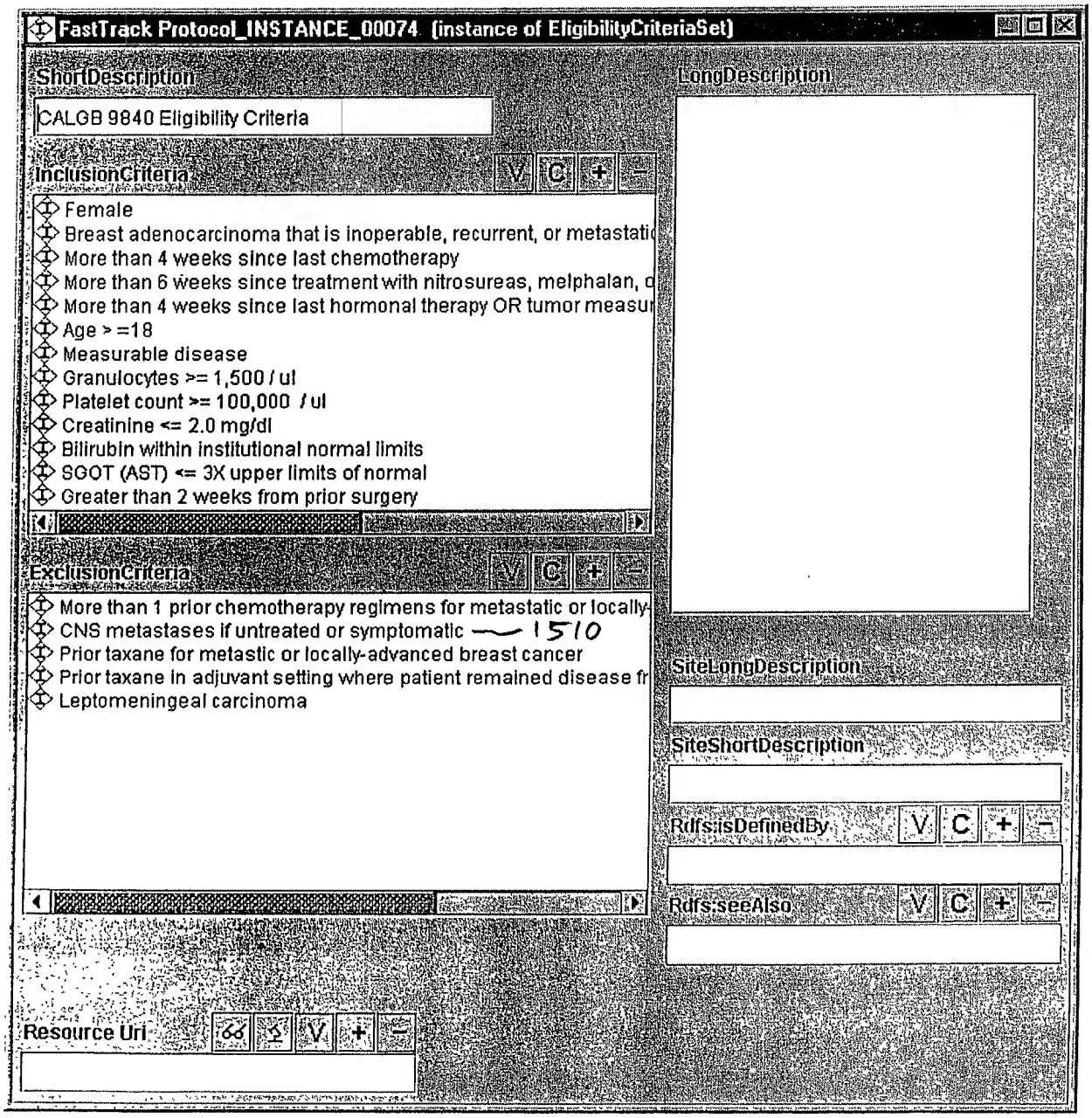


Fig. 15

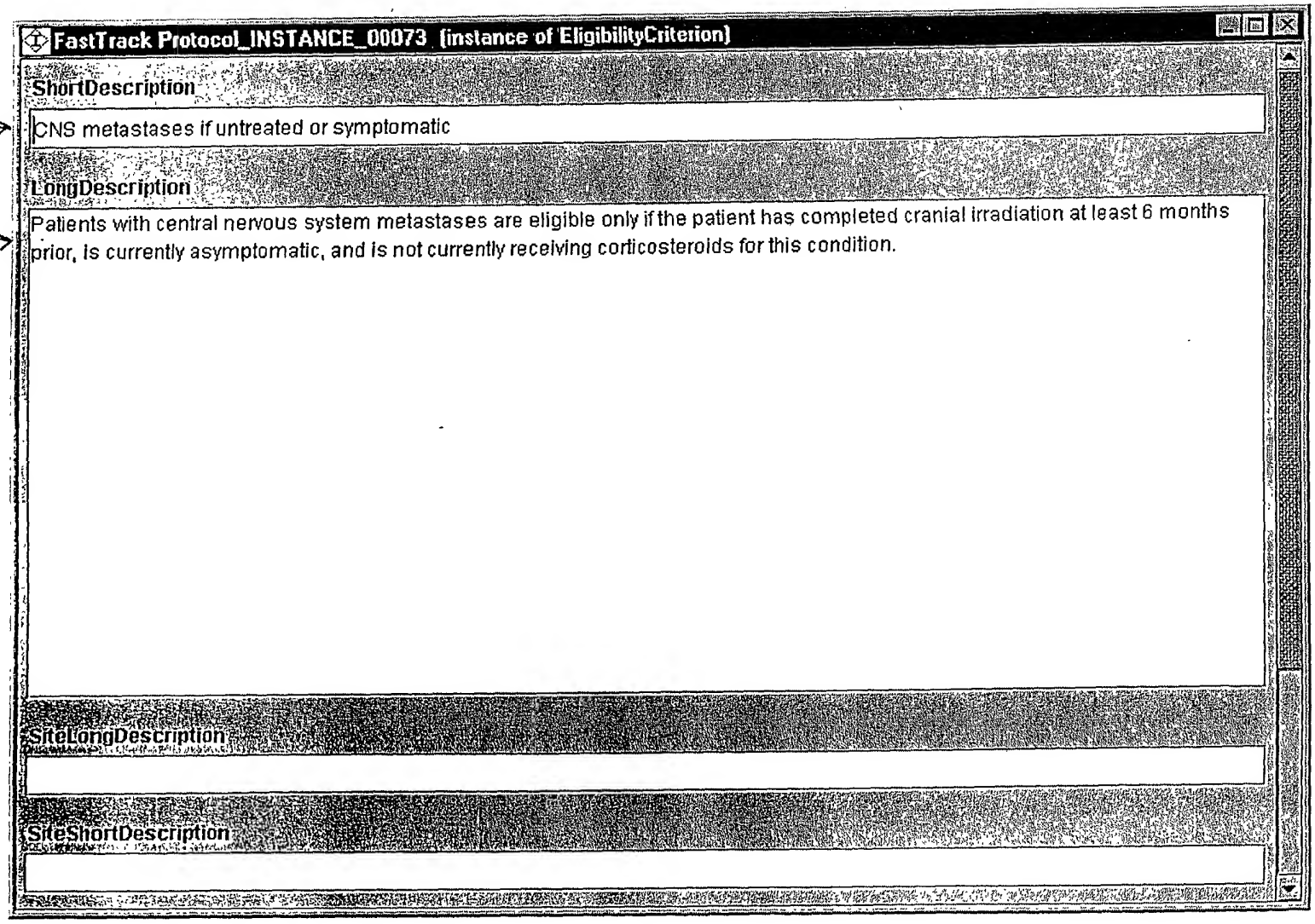

FastTrack Protocol_INSTANCE_00073 (instance of EligibilityCriterion)
ShortDescription
CNS metastases if untreated or symptomatic
LongDescription
Patients with central nervous system metastases are eligible only if the patient has completed cranial irradiation at least 6 months prior, is currently asymptomatic, and is not currently receiving corticosteroids for this condition.
SiteLongDescription
SiteShortDescription
1610
1612

Fig. 16

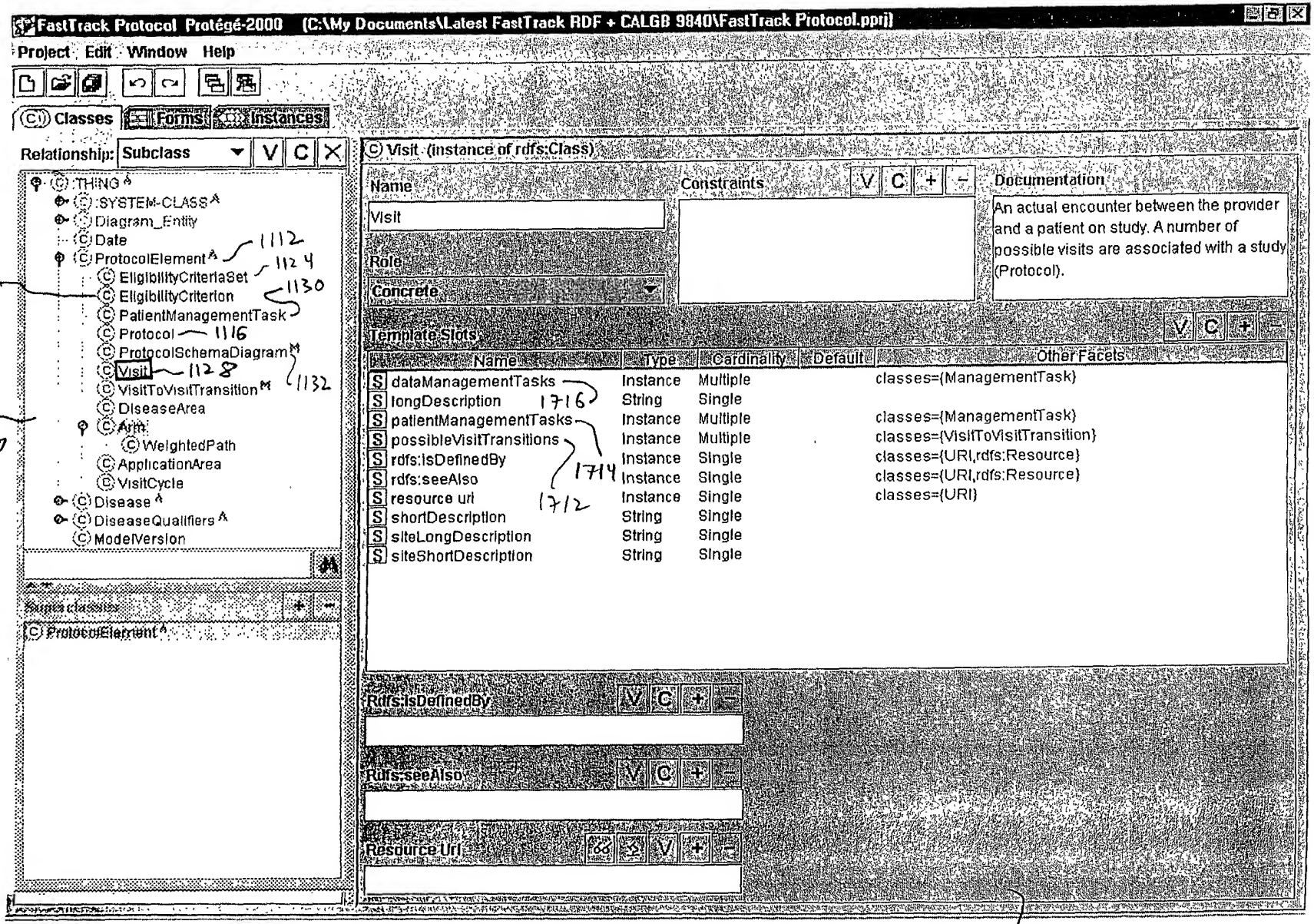


Fig. 17

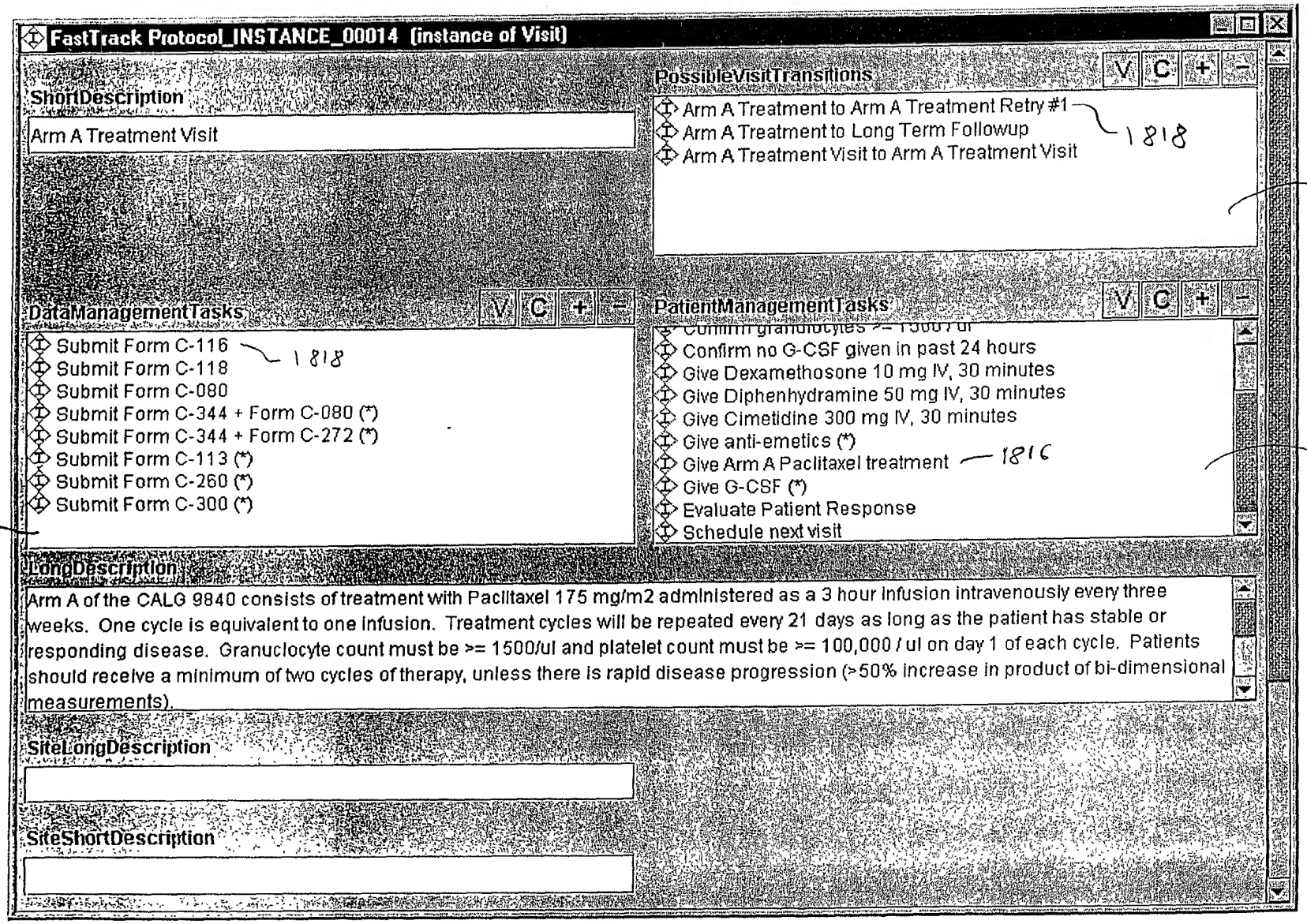

FastTrack Protocol_INSTANCE_00014 (instance of Visit)
ShortDescription
Arm A Treatment Visit
PossibleVisitTransitions
V C + −
Arm A Treatment to Arm A Treatment Retry #1
Arm A Treatment to Long Term Followup
Arm A Treatment Visit to Arm A Treatment Visit
1818
1810
DataManagementTasks
V C + −
Submit Form C-116
Submit Form C-118
Submit Form C-080
Submit Form C-344 + Form C-080 (*)
Submit Form C-344 + Form C-272 (*)
Submit Form C-113 (*)
Submit Form C-260 (*)
Submit Form C-300 (*)
1818
814
PatientManagementTasks
V C + −
Confirm granulocytes >= 1500/ ul
Confirm no G-CSF given in past 24 hours
Give Dexamethosone 10 mg IV, 30 minutes
Give Diphenhydramine 50 mg IV, 30 minutes
Give Cimetidine 300 mg IV, 30 minutes
Give anti-emetics (*)
Give Arm A Paclitaxel treatment
Give G-CSF (*)
Evaluate Patient Response
Schedule next visit
1816
1812
LongDescription
Arm A of the CALG 9840 consists of treatment with Paclitaxel 175 mg/m2 administered as a 3 hour infusion intravenously every three weeks. One cycle is equivalent to one infusion. Treatment cycles will be repeated every 21 days as long as the patient has stable or responding disease. Granuclocyte count must be >= 1500/ul and platelet count must be >= 100,000 / ul on day 1 of each cycle. Patients should receive a minimum of two cycles of therapy, unless there is rapid disease progression (>50% increase in product of bi-dimensional measurements).
SiteLongDescription
SiteShortDescription

Fig. 18

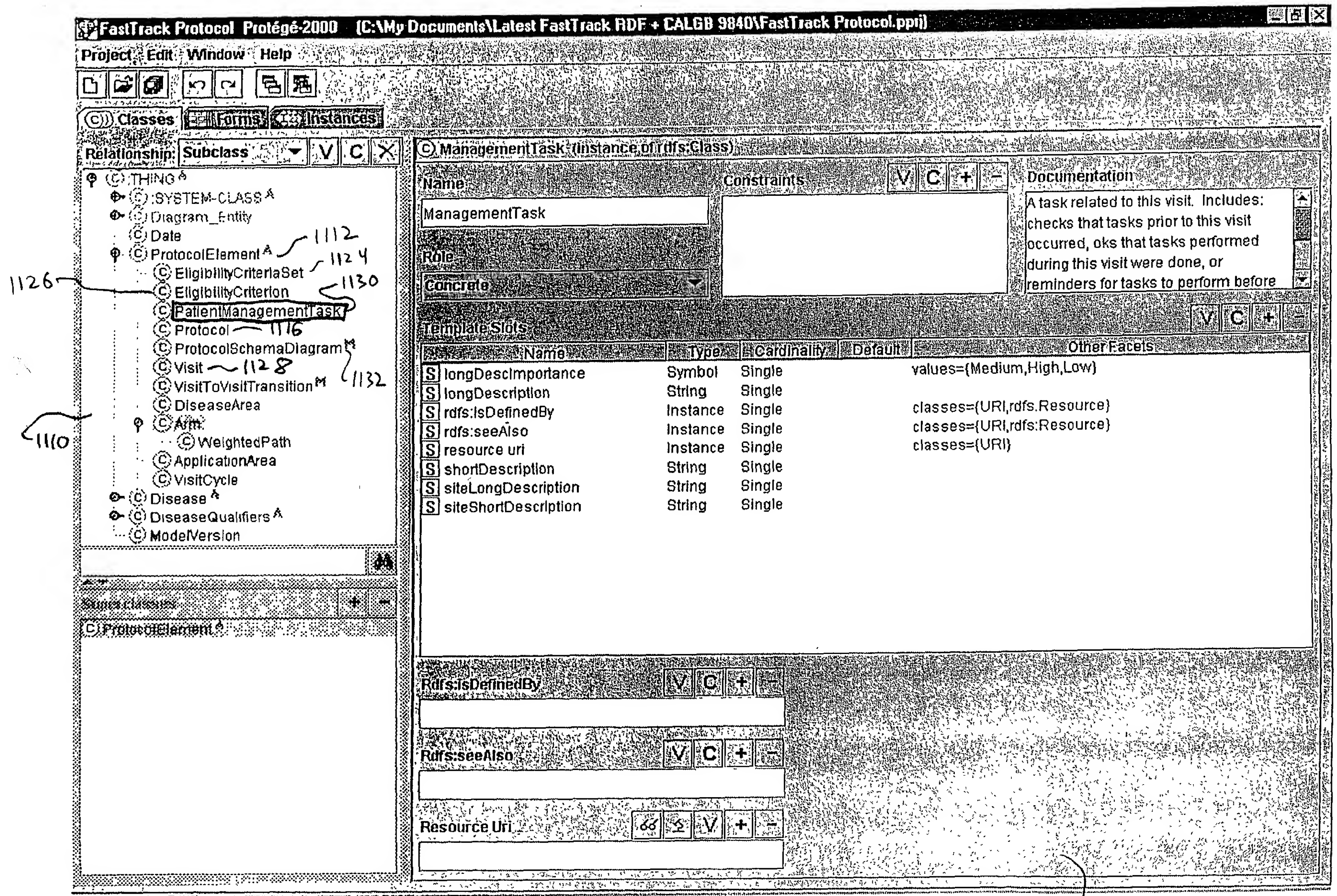

FastTrack Protocol Protégé-2000 (C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj)
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass
THING
:SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease
DiseaseQualifiers
ModelVersion
Superclasses
ProtocolElement
ManagementTask (instance of rdfs:Class)
Name
ManagementTask
Role
Concrete
Constraints
Documentation
A task related to this visit. Includes: checks that tasks prior to this visit occurred, oks that tasks performed during this visit were done, or reminders for tasks to perform before
Template Slots
Name Type Cardinality Default Other Facets
longDescImportance Symbol Single values={Medium,High,Low}
longDescription String Single
rdfs:isDefinedBy Instance Single classes={URI,rdfs.Resource}
rdfs:seeAlso Instance Single classes={URI,rdfs:Resource}
resource uri Instance Single classes={URI}
shortDescription String Single
siteLongDescription String Single
siteShortDescription String Single
Rdfs:isDefinedBy
Rdfs:seeAlso
Resource Uri
1110
1112
1116
1124
1126
1128
1130
1132
1910

Fig. 19

FastTrack Protocol_INSTANCE_00206 (instance of ManagementTask)

ShortDescription

Give Arm A Paclitaxel treatment

LongDescription

Give Paclitaxel 175 mg/m2 IV, 3 hours. This treatment is given to patients in Arm A of the CALGB 9840 protocol. It is given once every 3 weeks. One cycle is equivalent to one infusion. Granuclocyte count must be >= 1500/ul and platelet count must be >= 100,000 / ul on day 1 of each cycle in order to proceed with the Paclitaxel infusion. Patients must receive the pre-medication prior to Paclitaxel infusion. If either the granulocyte or platelet count are not adequate, do not continue with treatment. Patients should receive a minimum of 2 cycles unless there is rapid disease progression.

Expected toxicities:

Dose Modfications:

SiteLongDescription

Fig. 20

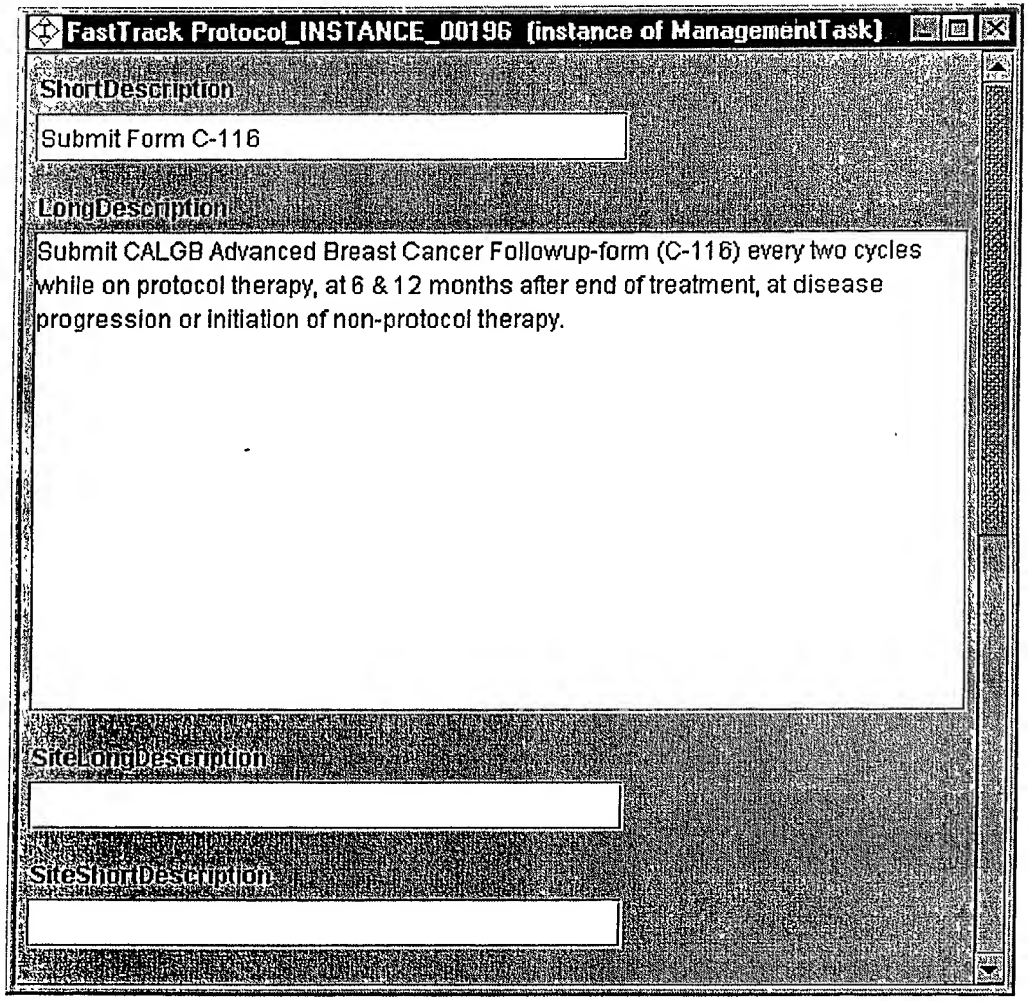

FastTrack Protocol_INSTANCE_00196 (instance of ManagementTask)
ShortDescription
Submit Form C-116
LongDescription
Submit CALGB Advanced Breast Cancer Followup-form (C-116) every two cycles while on protocol therapy, at 6 & 12 months after end of treatment, at disease progression or initiation of non-protocol therapy.
SiteLongDescription
SiteShortDescription

Fig. 21

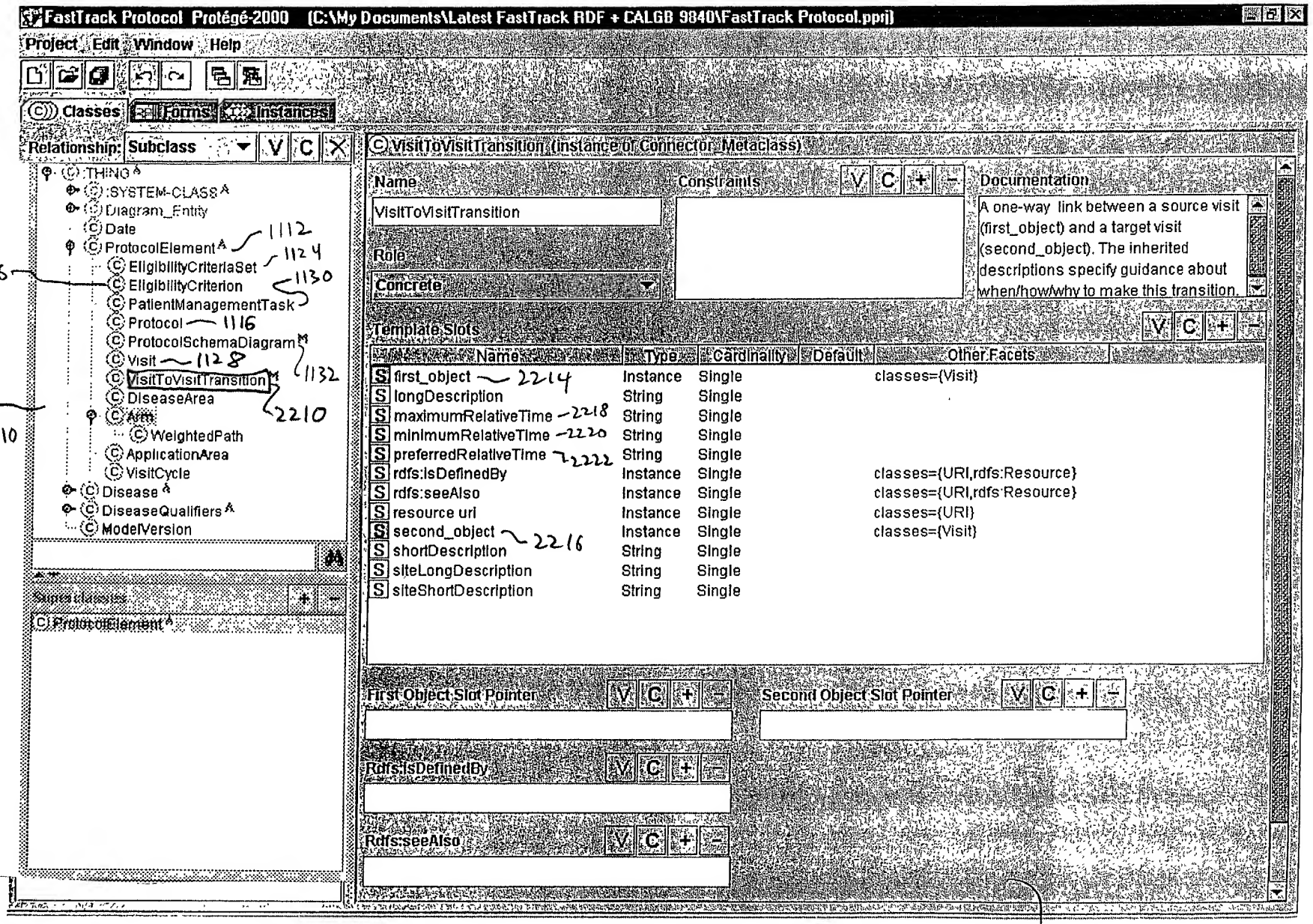


Fig. 22

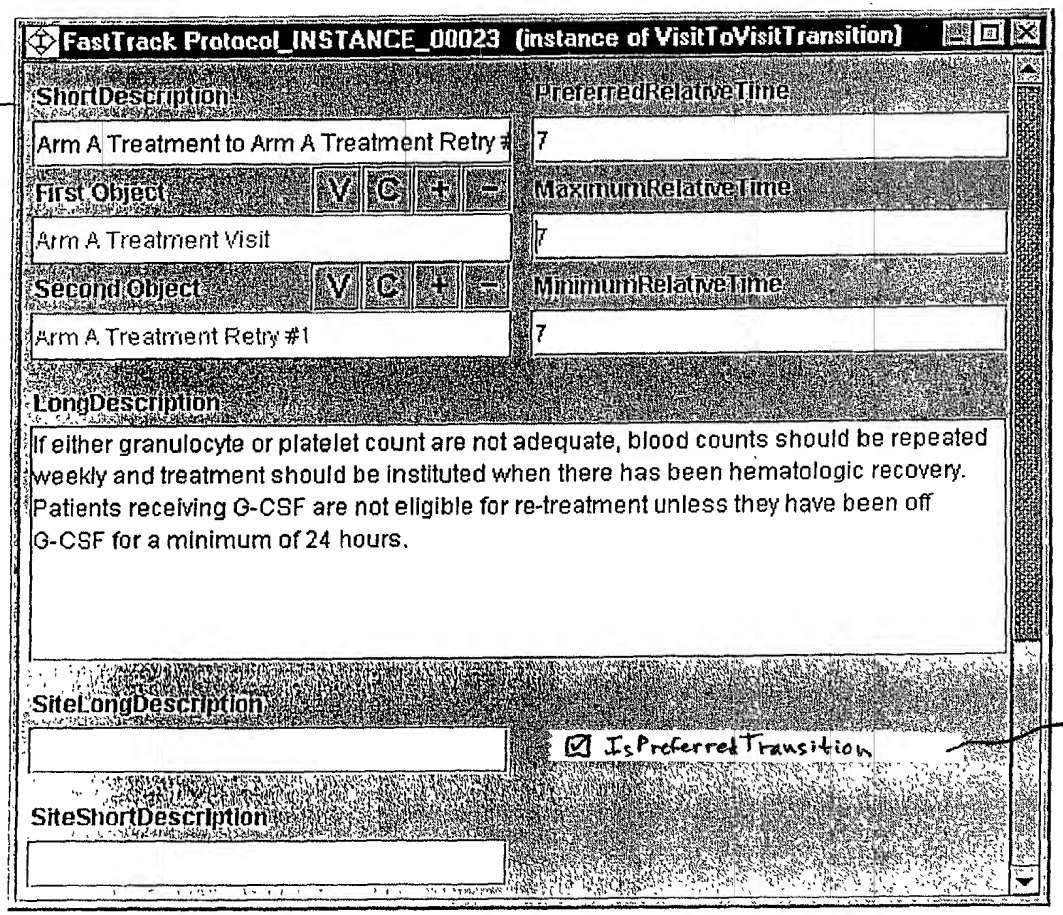


Fig. 23

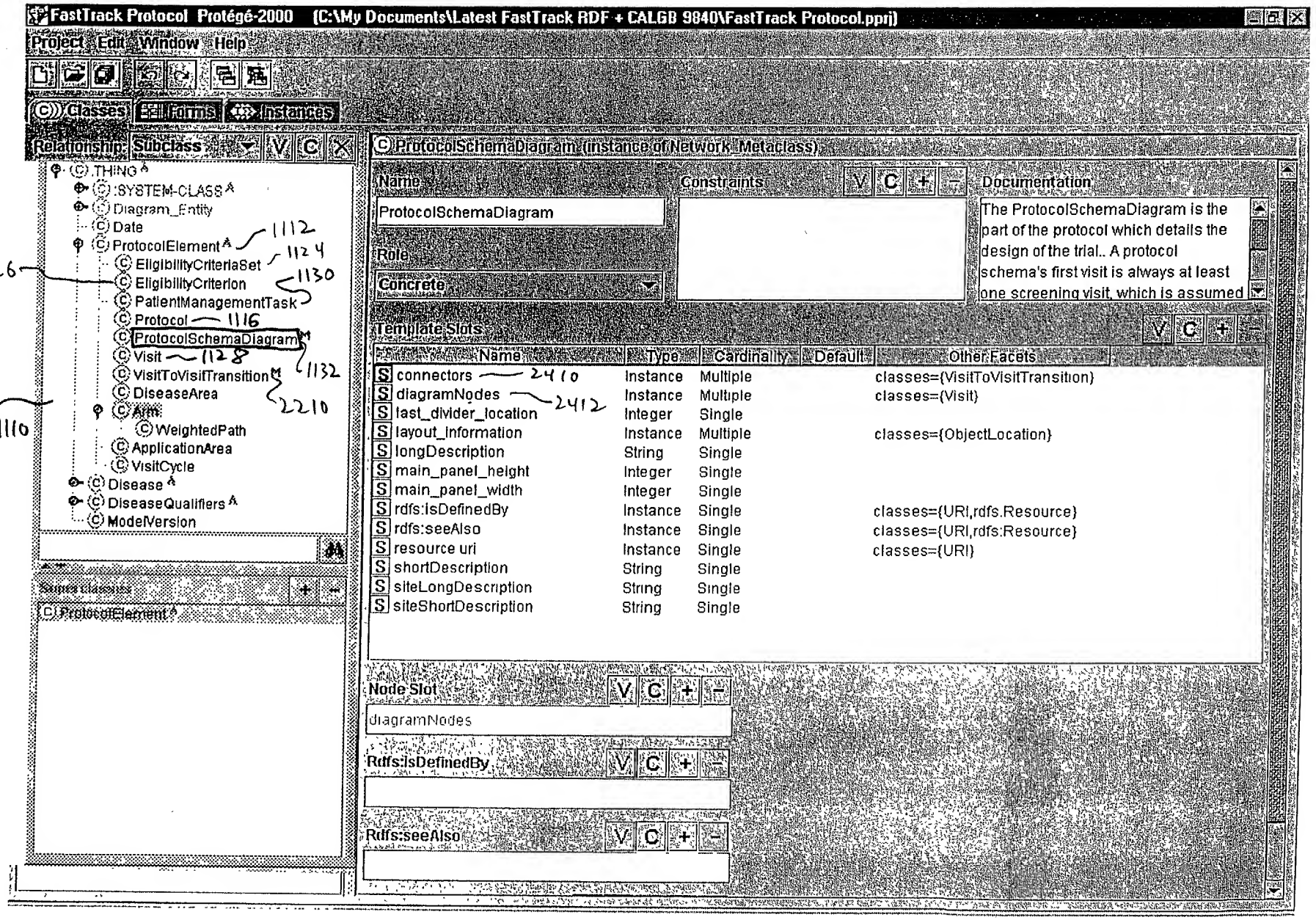


Fig. 24

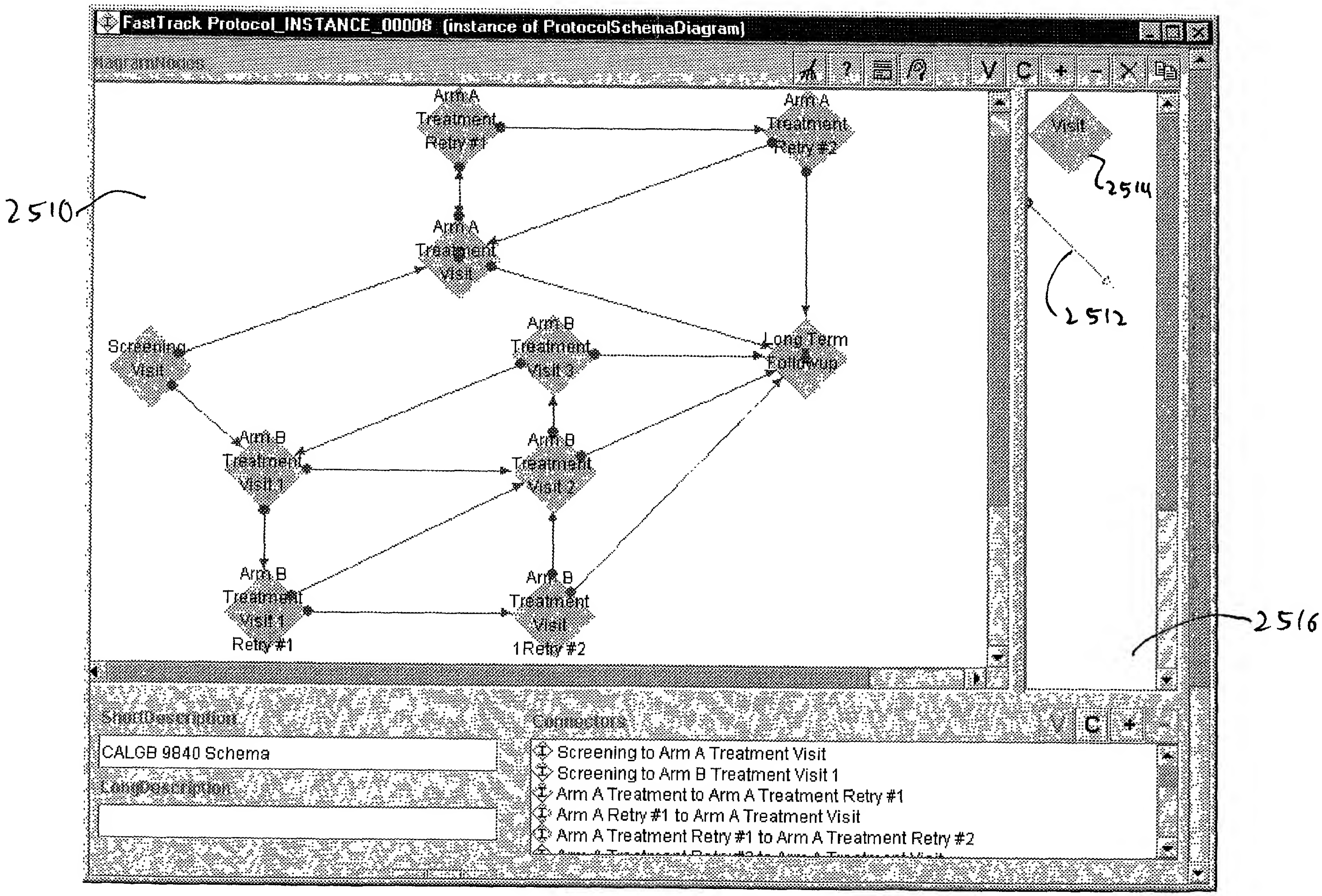

FastTrack Protocol_INSTANCE_00008 (instance of ProtocolSchemaDiagram)
Arm A Treatment Retry #1
Arm A Treatment Retry #2
Arm A Treatment Visit
Screening Visit
Arm B Treatment Visit 3
Long Term Followup
Arm B Treatment Visit 1
Arm B Treatment Visit 2
Arm B Treatment Visit 1 Retry #1
Arm B Treatment Visit 1Retry #2
Visit
2510
2512
2514
2516
ShortDescription
CALGB 9840 Schema
LongDescription
Connectors
Screening to Arm A Treatment Visit
Screening to Arm B Treatment Visit 1
Arm A Treatment to Arm A Treatment Retry #1
Arm A Retry #1 to Arm A Treatment Visit
Arm A Treatment Retry #1 to Arm A Treatment Retry #2

Fig. 25

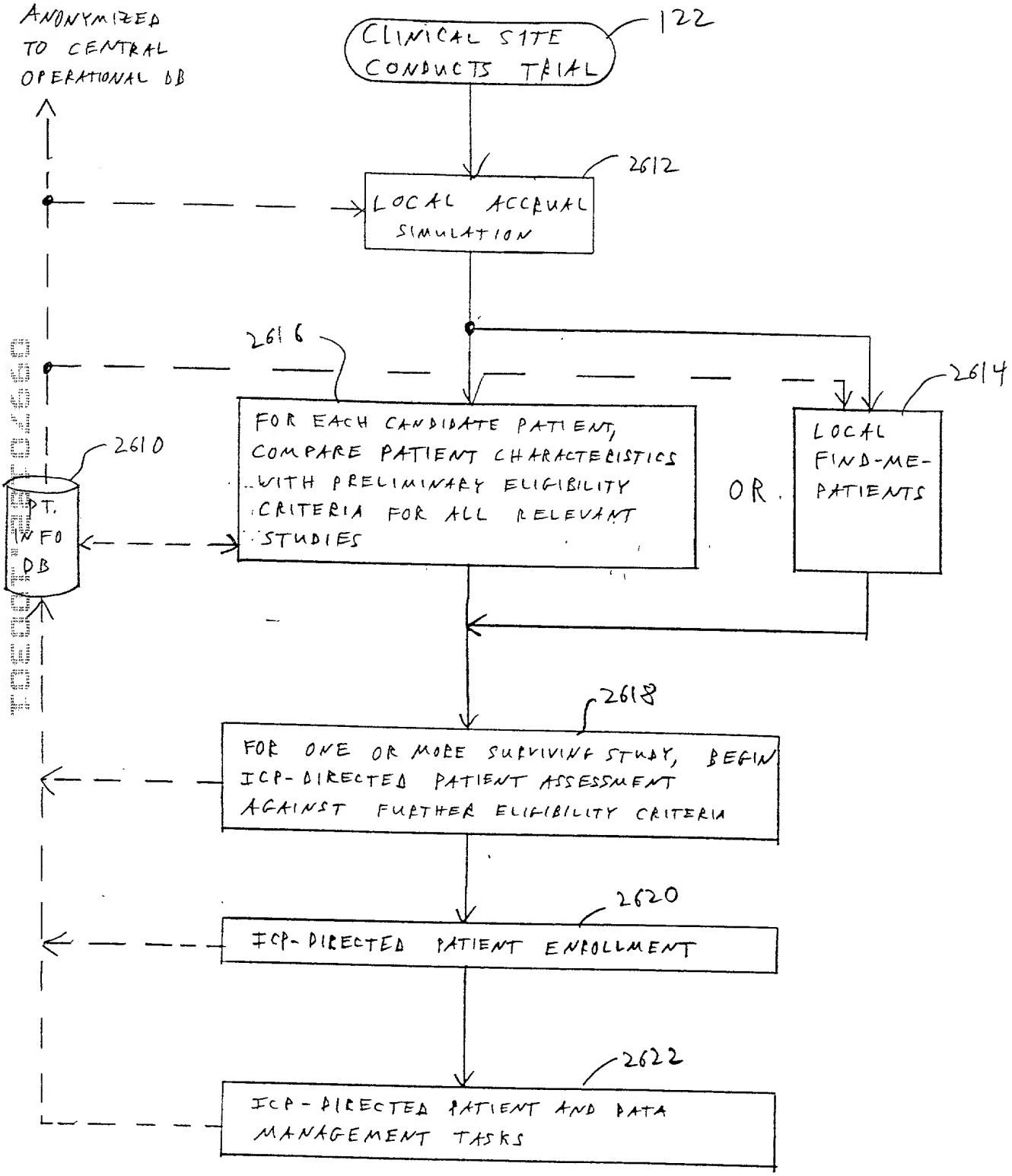

ANONYMIZED TO CENTRAL OPERATIONAL DB
CLINICAL SITE CONDUCTS TRIAL
122
2612
LOCAL ACCRUAL SIMULATION
2616
FOR EACH CANDIDATE PATIENT, COMPARE PATIENT CHARACTERISTICS WITH PRELIMINARY ELIGIBILITY CRITERIA FOR ALL RELEVANT STUDIES
OR
2614
LOCAL FIND-ME-PATIENTS
2610
T. INFO DB
2618
FOR ONE OR MORE SURVIVING STUDY, BEGIN ICP-DIRECTED PATIENT ASSESSMENT AGAINST FURTHER ELIGIBILITY CRITERIA
2620
ICP-DIRECTED PATIENT ENROLLMENT
2622
ICP-DIRECTED PATIENT AND DATA MANAGEMENT TASKS

Fig. 26

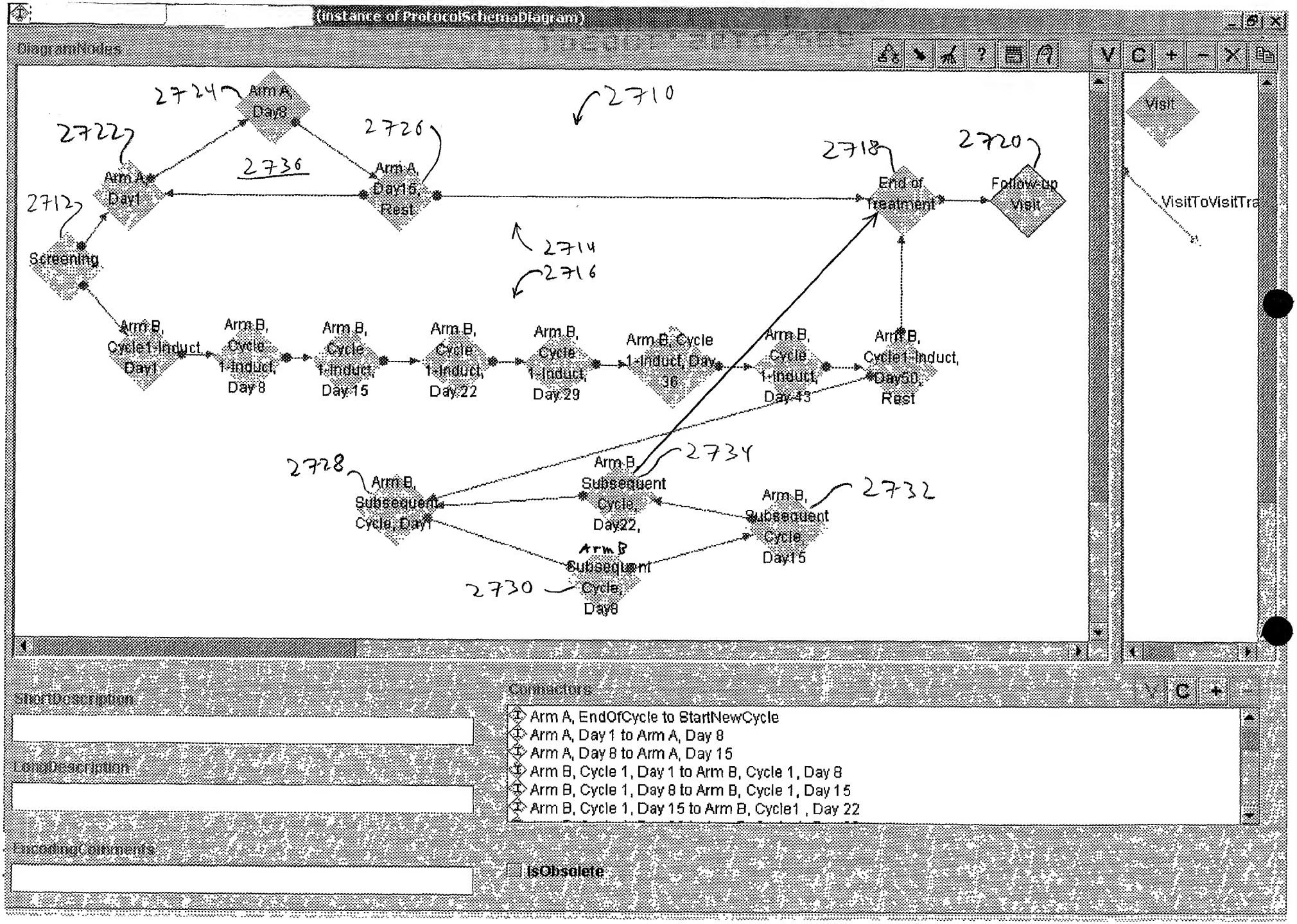

(Instance of ProtocolSchemaDiagram)
Diagram Nodes
2724
Arm A, Day8
2710
2722
2726
2736
Arm A, Day1
Arm A, Day15, Rest
2718
2720
End of Treatment
Follow-up Visit
Visit
VisitToVisitTra
2712
Screening
2714
2716
Arm B, Cycle1-Induct, Day1
Arm B, Cycle 1-Induct, Day 8
Arm B, Cycle 1-Induct, Day 15
Arm B, Cycle 1-Induct, Day 22
Arm B, Cycle 1-Induct, Day 29
Arm B, Cycle 1-Induct, Day 36
Arm B, Cycle 1-Induct, Day 43
Arm B, Cycle1-Induct, Day50, Rest
2728
2734
Arm B, Subsequent Cycle, Day1
Arm B, Subsequent Cycle, Day22,
Arm B, Subsequent Cycle, Day15
2732
Arm B Subsequent Cycle, Day8
2730
StartDescription
LongDescription
EncodingComments
Connectors
Arm A, EndOfCycle to StartNewCycle
Arm A, Day 1 to Arm A, Day 8
Arm A, Day 8 to Arm A, Day 15
Arm B, Cycle 1, Day 1 to Arm B, Cycle 1, Day 8
Arm B, Cycle 1, Day 8 to Arm B, Cycle 1, Day 15
Arm B, Cycle 1, Day 15 to Arm B, Cycle1 , Day 22
IsObsolete

Fig. 27

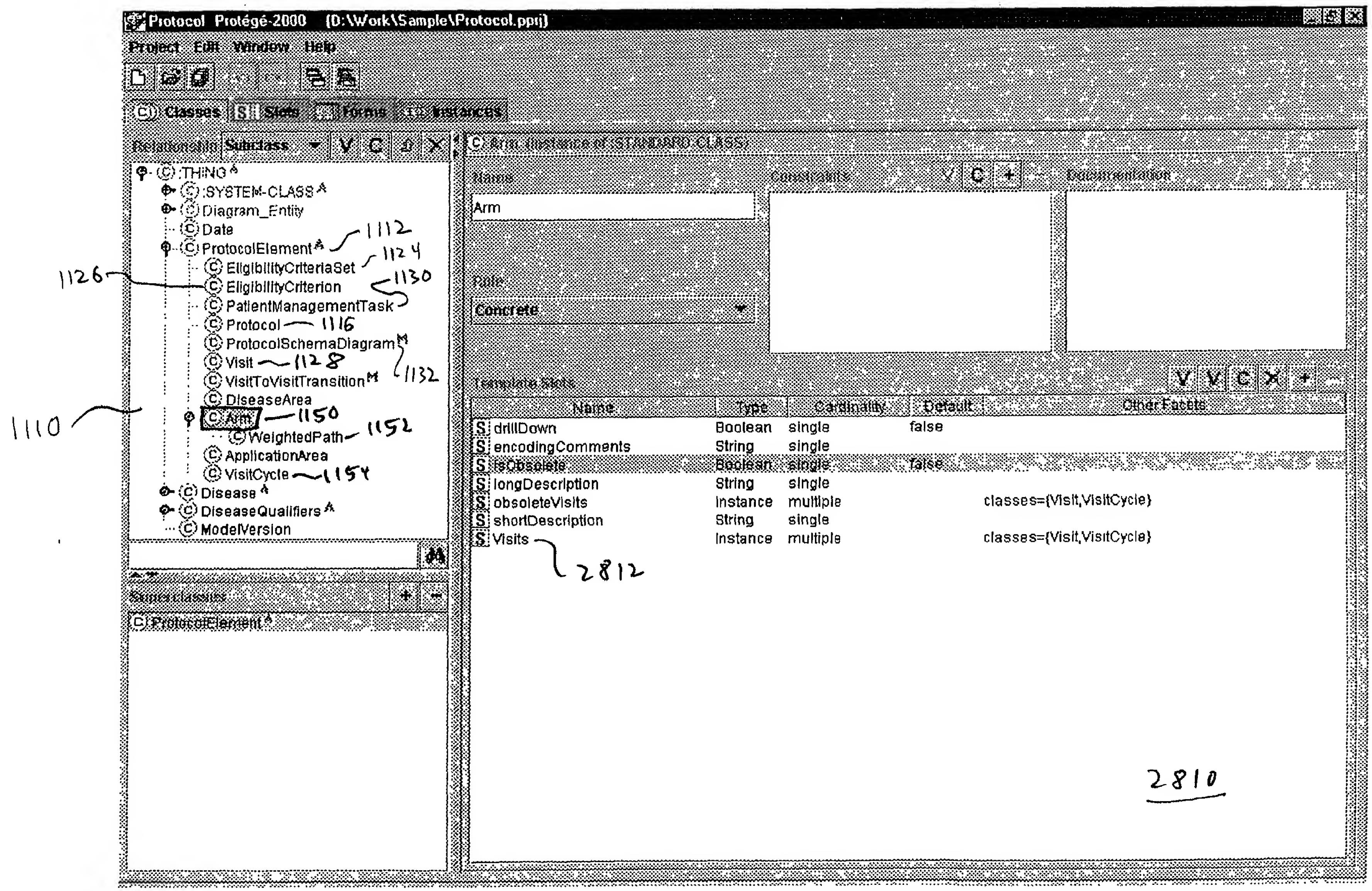

Protocol Protégé-2000 (D:\Work\Sample\Protocol.pprj)
Project Edit Window Help
Classes Slots Forms Instances
Relationship Subclass
:THING
:SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
1112
EligibilityCriteriaSet
1124
EligibilityCriterion
1126
1130
PatientManagementTask
Protocol
1116
ProtocolSchemaDiagram
Visit
1128
VisitToVisitTransition
1132
DiseaseArea
Arm
1110
1150
WeightedPath
1152
ApplicationArea
VisitCycle
1154
Disease
DiseaseQualifiers
ModelVersion
Superclasses
ProtocolElement
Arm (instance of :STANDARD-CLASS)
Name
Arm
Constraints
Documentation
Role
Concrete
Template Slots
Name Type Cardinality Default Other Facets
drillDown Boolean single false
encodingComments String single
isObsolete Boolean single false
longDescription String single
obsoleteVisits Instance multiple classes={Visit,VisitCycle}
shortDescription String single
Visits Instance multiple classes={Visit,VisitCycle}
2812
2810

Fig. 28

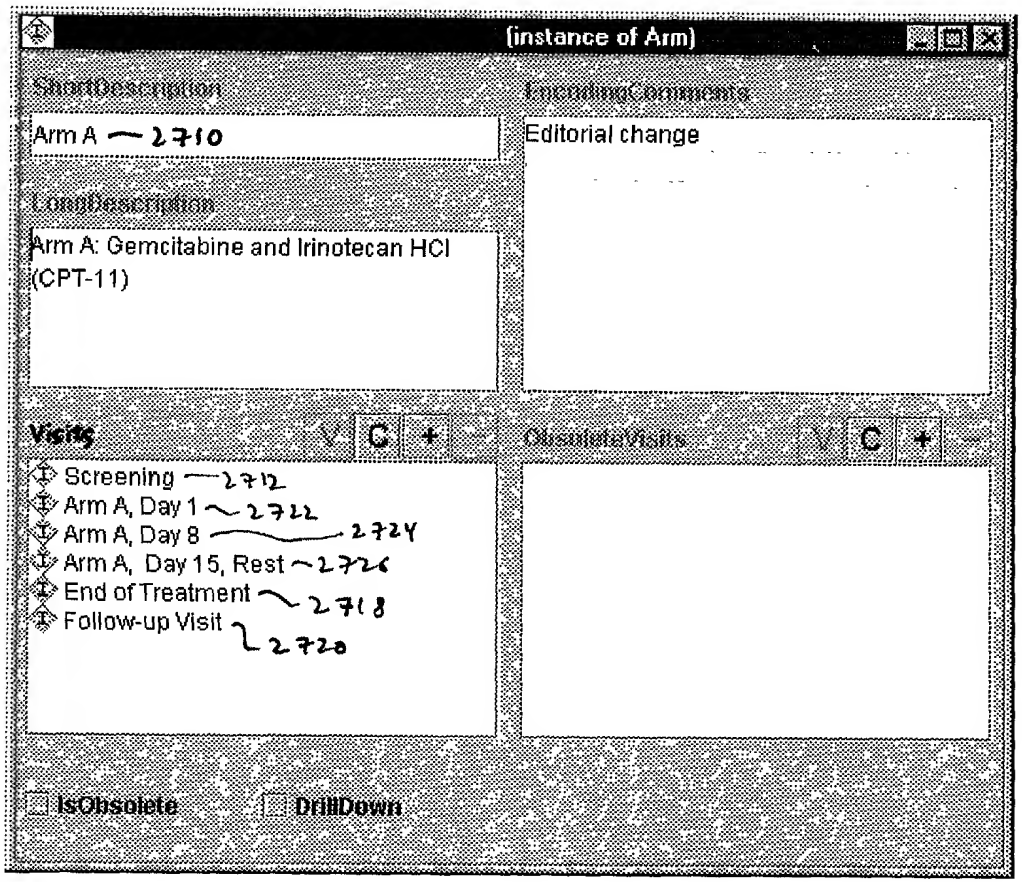


Fig. 29

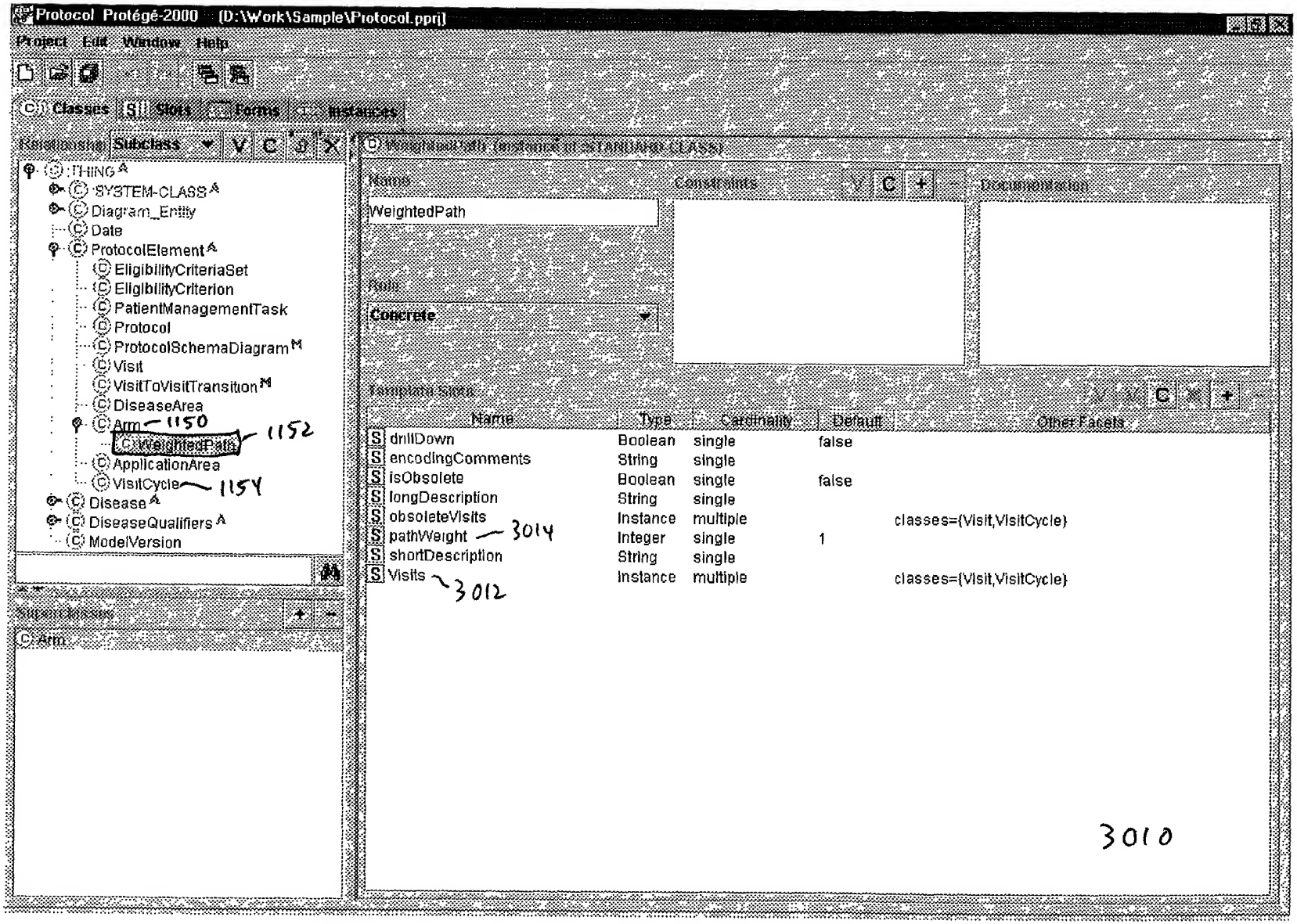

Protocol Protégé-2000 (D:\Work\Sample\Protocol.pprj)
Project Edit Window Help
Classes Slots Forms Instances
Relationship: Subclass
THING
SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease
DiseaseQualifiers
ModelVersion
Superclasses:
Arm
Name:
WeightedPath
Constraints:
Documentation:
Role:
Concrete
Template Slots:
Name
Type
Cardinality
Default
Other Facets
drillDown Boolean single false
encodingComments String single
isObsolete Boolean single false
longDescription String single
obsoleteVisits Instance multiple classes={Visit,VisitCycle}
pathWeight Integer single 1
shortDescription String single
Visits Instance multiple classes={Visit,VisitCycle}
1150
1152
1154
3014
3012
3010

Fig. 30

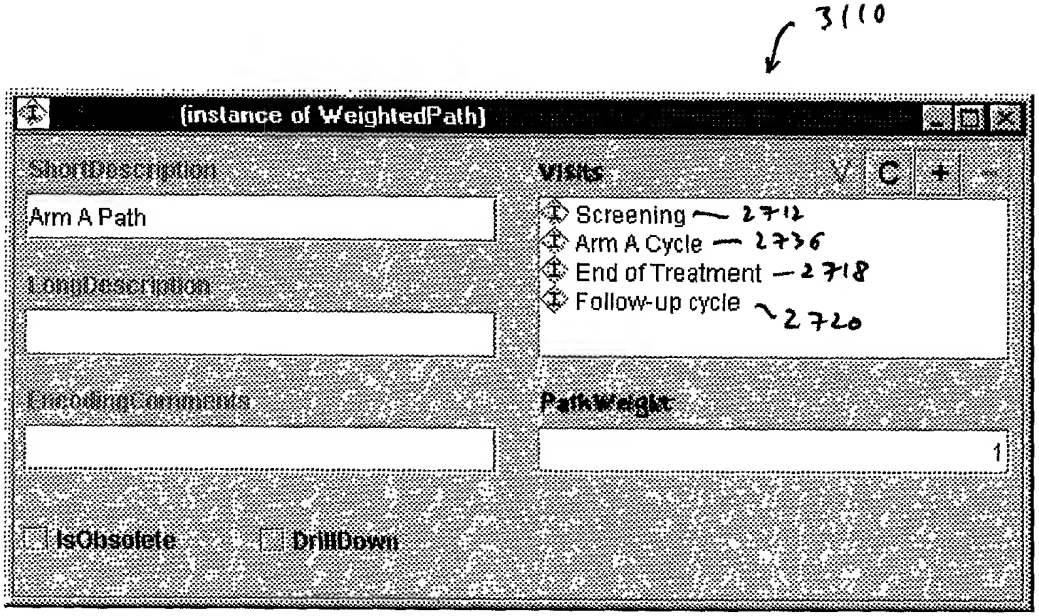


Fig. 31

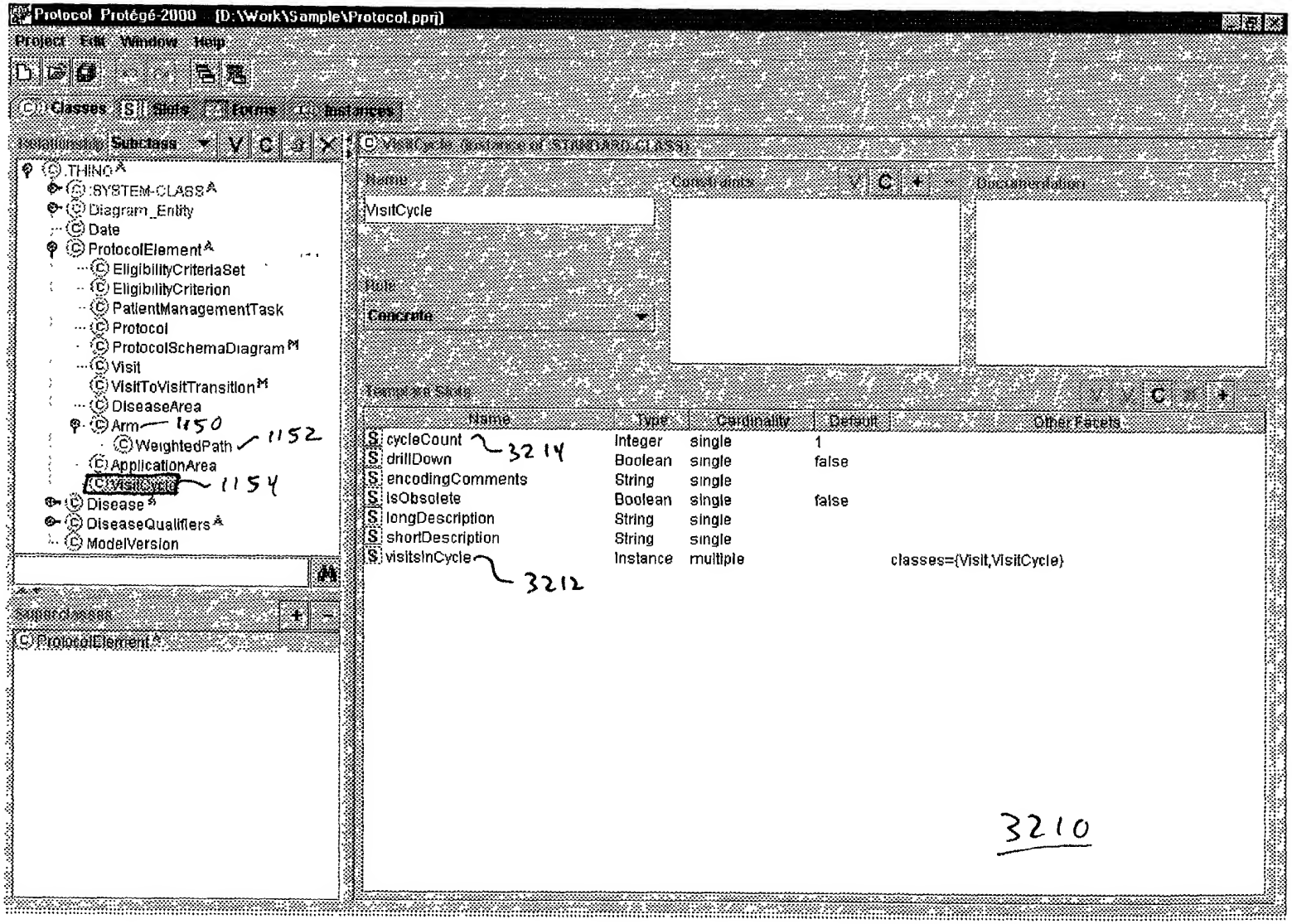

Protocol Protégé-2000 [D:\Work\Sample\Protocol.pprj]
Project Edit Window Help
Classes Slots Forms Instances
Subclass
THING
SYSTEM-CLASS
Diagram_Entity
Date
ProtocolElement
EligibilityCriteriaSet
EligibilityCriterion
PatientManagementTask
Protocol
ProtocolSchemaDiagram
Visit
VisitToVisitTransition
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease
DiseaseQualifiers
ModelVersion
Superclasses
ProtocolElement
Name
VisitCycle
Role
Concrete
Constraints
Documentation
Template Slots
Name
Type
Cardinality
Default
Other Facets
cycleCount
integer
single
1
drillDown
Boolean
single
false
encodingComments
String
single
isObsolete
Boolean
single
false
longDescription
String
single
shortDescription
String
single
visitsInCycle
Instance
multiple
classes={Visit,VisitCycle}
1150
1152
1154
3214
3212
3210

Fig. 32

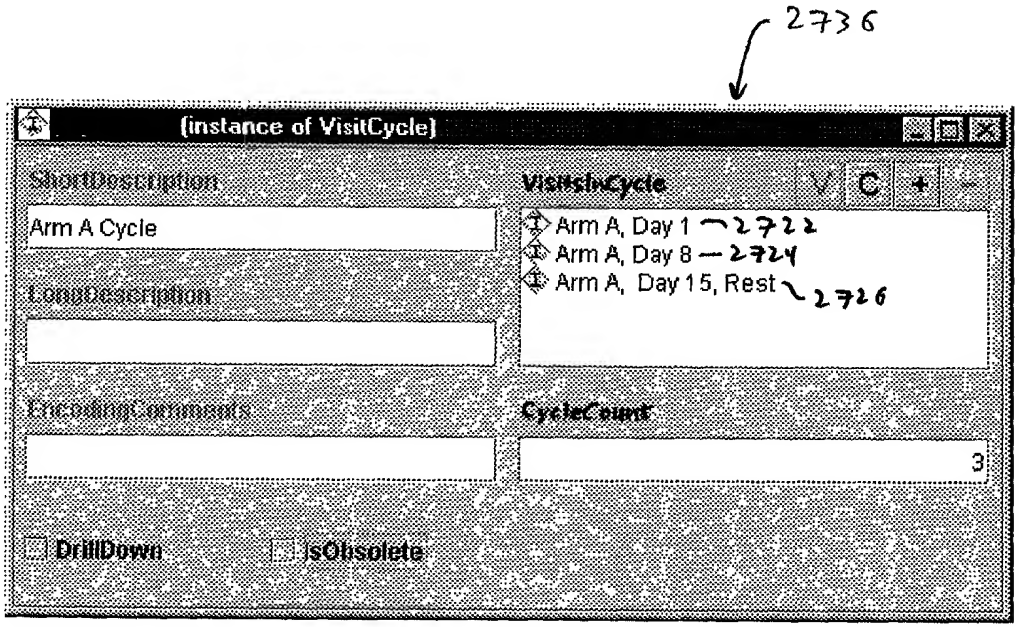


Fig. 33

Timeline Simulation Process Flow

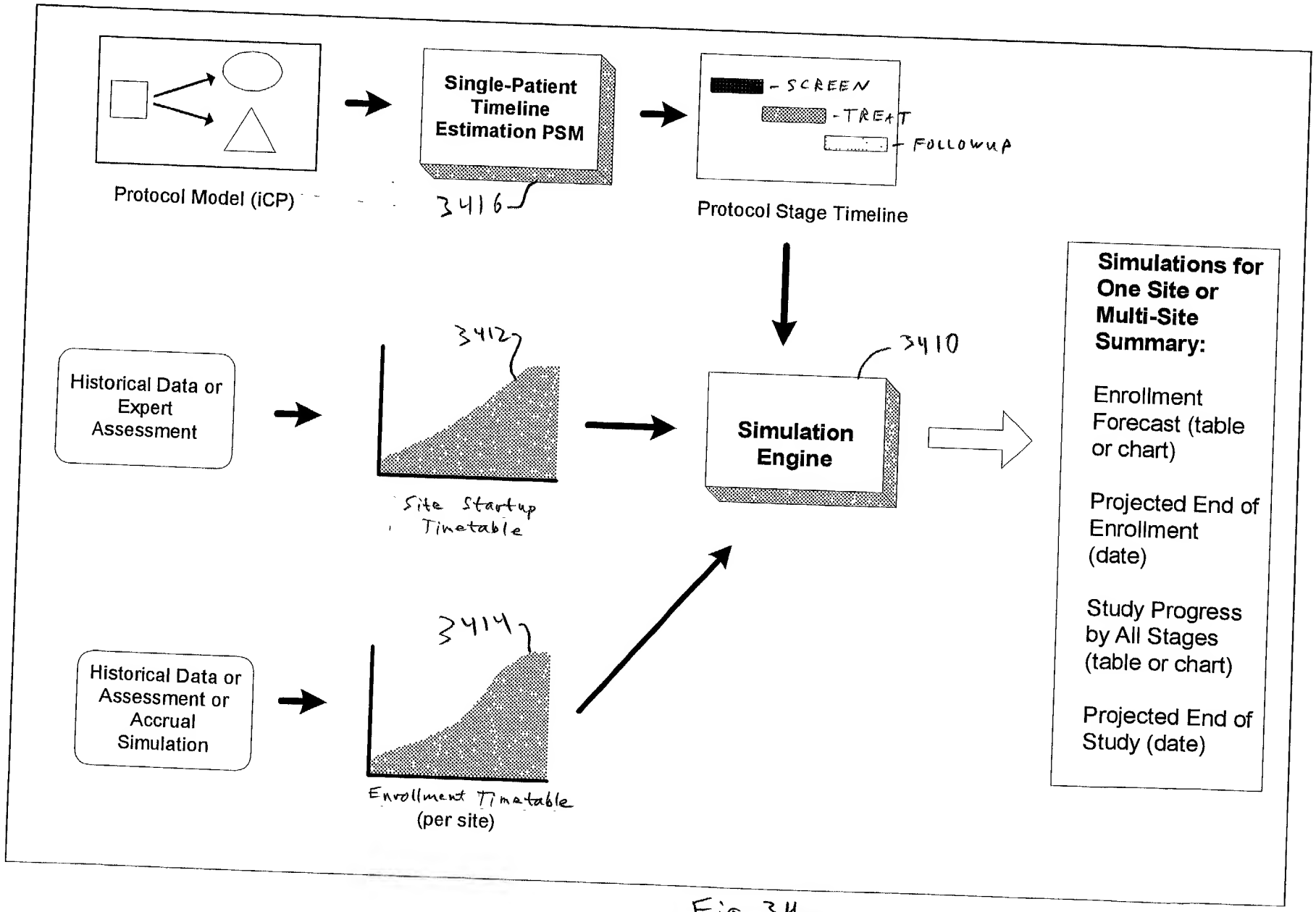


Fig. 34

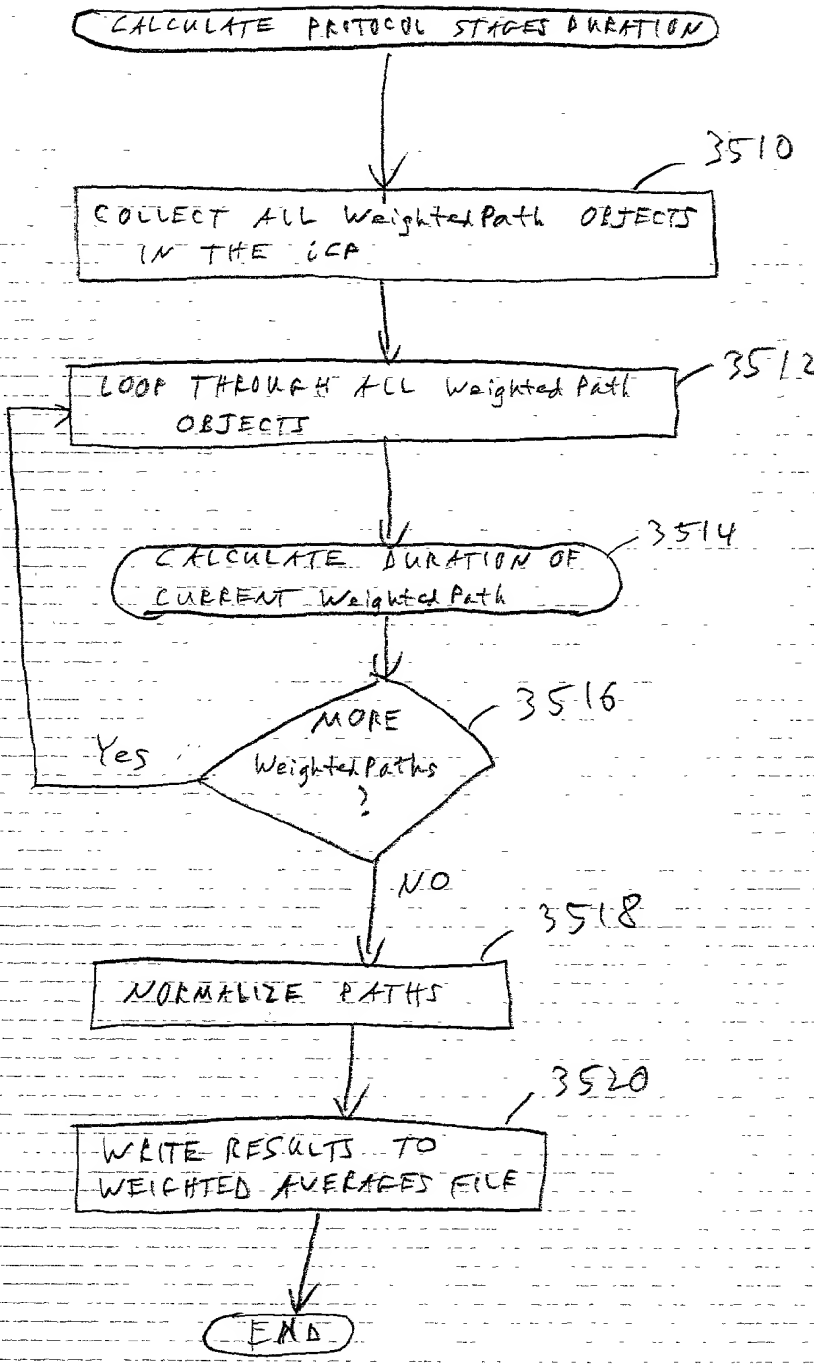

CALCULATE PROTOCOL STAGES DURATION
3510
COLLECT ALL WeightedPath OBJECTS IN THE ICP
3512
LOOP THROUGH ALL WeightedPath OBJECTS
3514
CALCULATE DURATION OF CURRENT WeightedPath
3516
MORE WeightedPaths ?
Yes
NO
3518
NORMALIZE PATHS
3520
WRITE RESULTS TO WEIGHTED AVERAGES FILE
END

Fig. 35

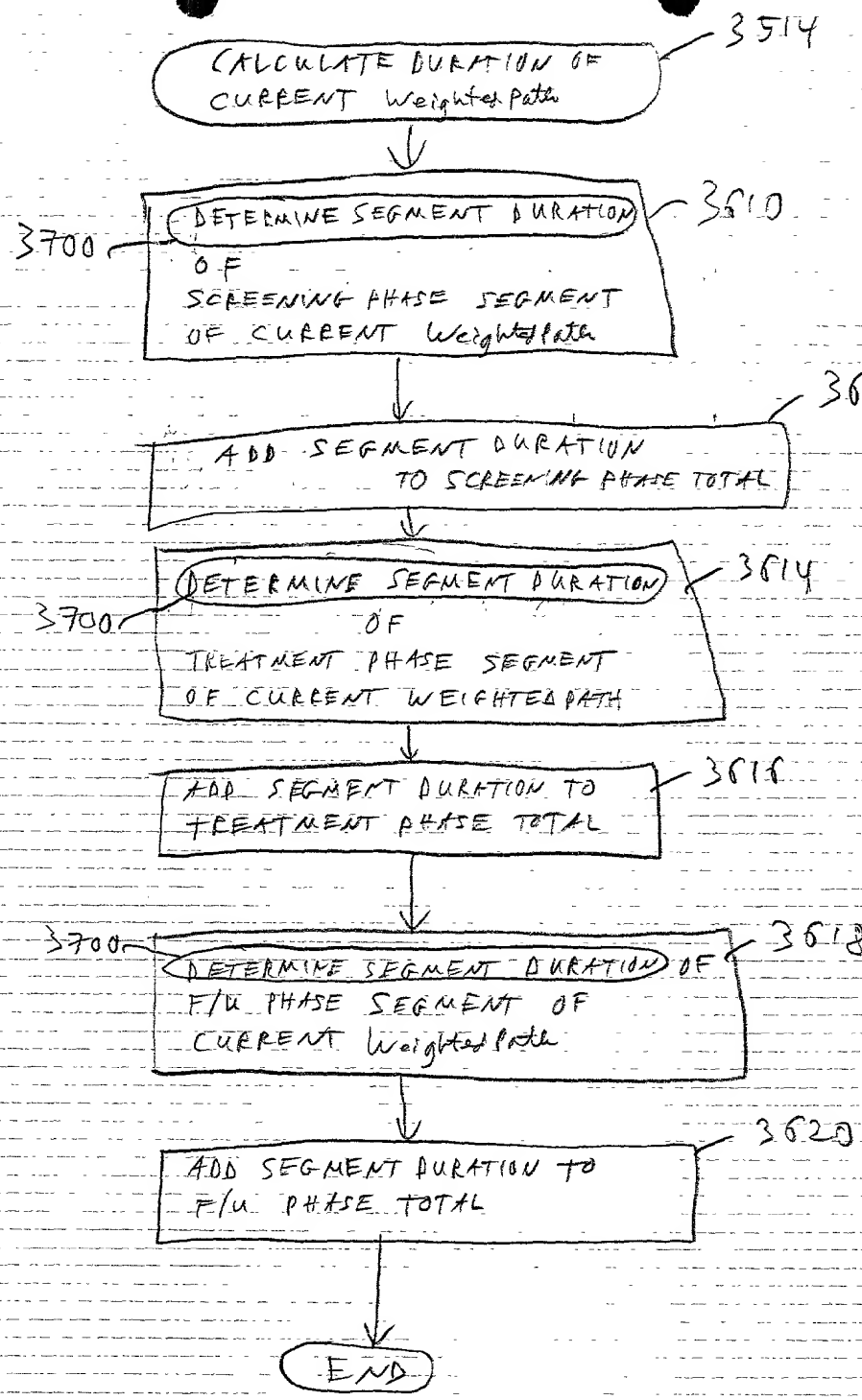

CALCULATE DURATION OF CURRENT Weighted Path
3514
DETERMINE SEGMENT DURATION OF SCREENING PHASE SEGMENT OF CURRENT Weighted Path
3510
3700
ADD SEGMENT DURATION TO SCREENING PHASE TOTAL
3612
DETERMINE SEGMENT DURATION OF TREATMENT PHASE SEGMENT OF CURRENT WEIGHTED PATH
3614
3700
ADD SEGMENT DURATION TO TREATMENT PHASE TOTAL
3616
DETERMINE SEGMENT DURATION OF F/U PHASE SEGMENT OF CURRENT Weighted Path
3618
3700
ADD SEGMENT DURATION TO F/U PHASE TOTAL
3620
END

Fig. 36

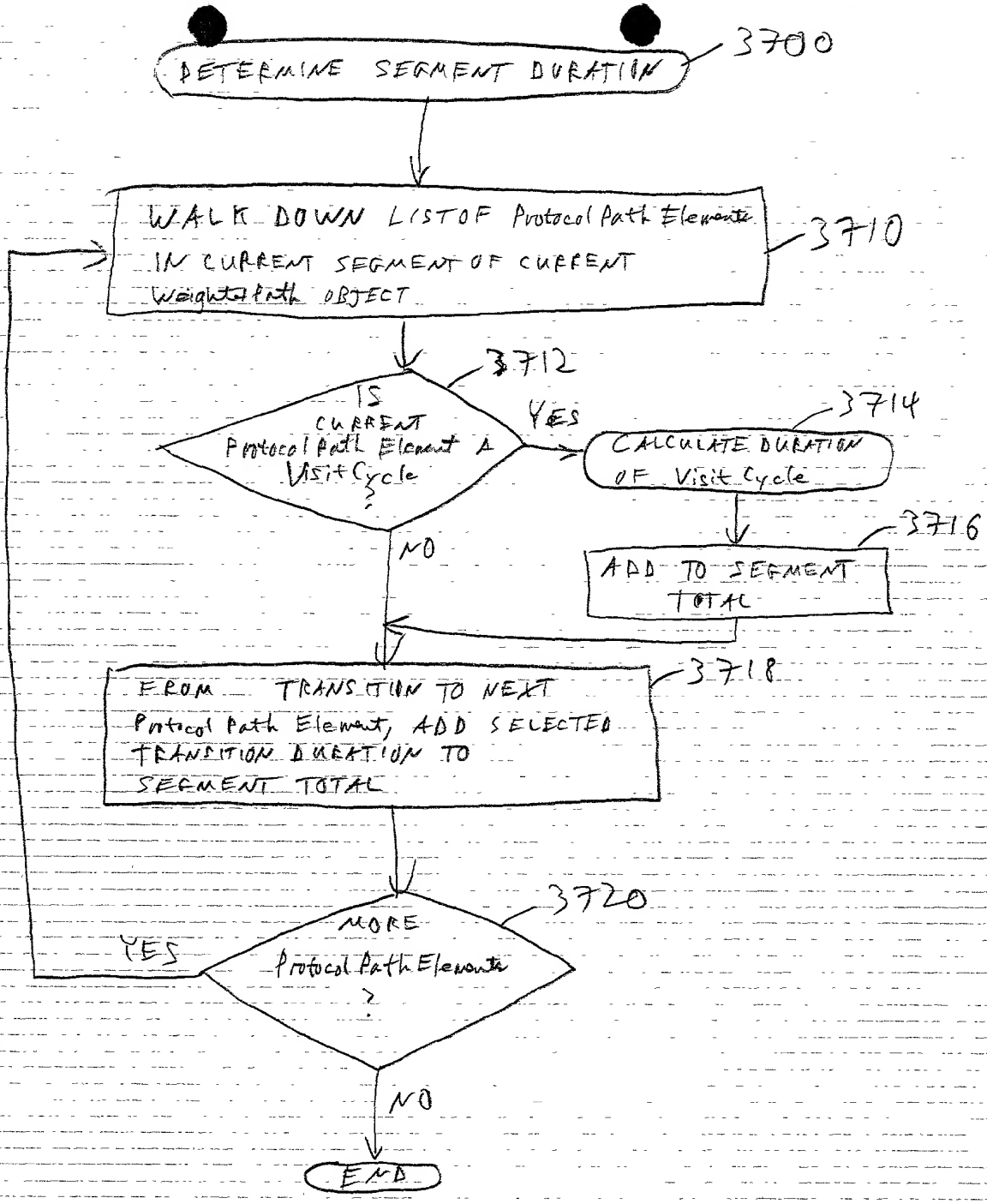

DETERMINE SEGMENT DURATION
3700
WALK DOWN LIST OF Protocol Path Elements IN CURRENT SEGMENT OF CURRENT Weighted Path OBJECT
3710
3712
IS CURRENT Protocol Path Element A Visit Cycle ?
YES
3714
CALCULATE DURATION OF Visit Cycle
3716
ADD TO SEGMENT TOTAL
NO
3718
FROM TRANSITION TO NEXT Protocol Path Element, ADD SELECTED TRANSITION DURATION TO SEGMENT TOTAL
3720
MORE Protocol Path Elements ?
YES
NO
END

Fig. 37

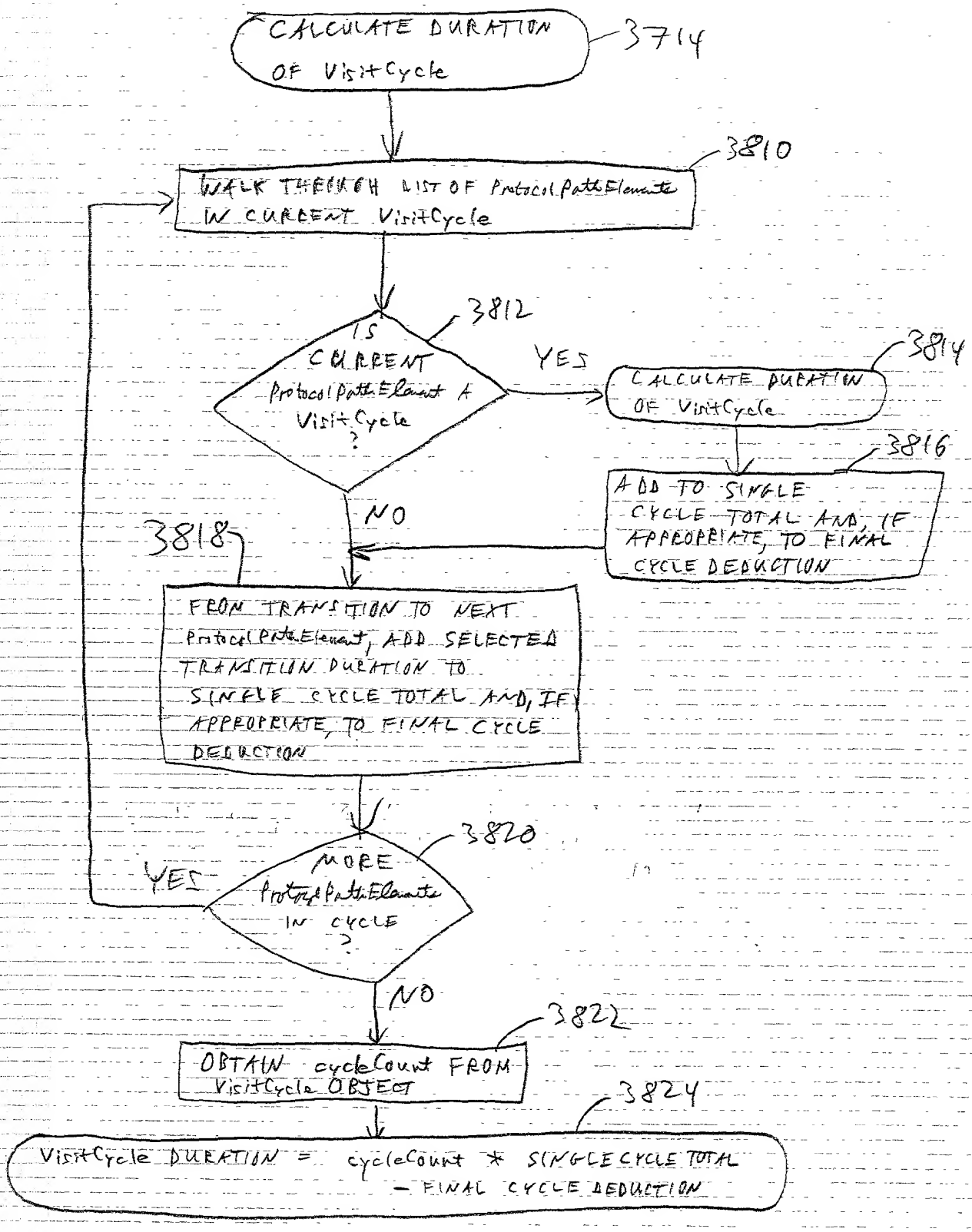

CALCULATE DURATION OF VisitCycle
3714
WALK THROUGH LIST OF ProtocolPathElements IN CURRENT VisitCycle
3810
IS CURRENT ProtocolPathElement A VisitCycle ?
3812
YES
CALCULATE DURATION OF VisitCycle
3814
ADD TO SINGLE CYCLE TOTAL AND, IF APPROPRIATE, TO FINAL CYCLE DEDUCTION
3816
NO
FROM TRANSITION TO NEXT ProtocolPathElement, ADD SELECTED TRANSITION DURATION TO SINGLE CYCLE TOTAL AND, IF APPROPRIATE, TO FINAL CYCLE DEDUCTION
3818
MORE ProtocolPathElements IN CYCLE ?
3820
YES
NO
OBTAIN cycleCount FROM VisitCycle OBJECT
3822
VisitCycle DURATION = cycleCount * SINGLE CYCLE TOTAL - FINAL CYCLE DEDUCTION
3824

Fig. 38

Screening duration = 7 + 7 = 14
Treatment = 3*(1+1+1) – 1+ 7 + 7 = 22
Follow up = 30

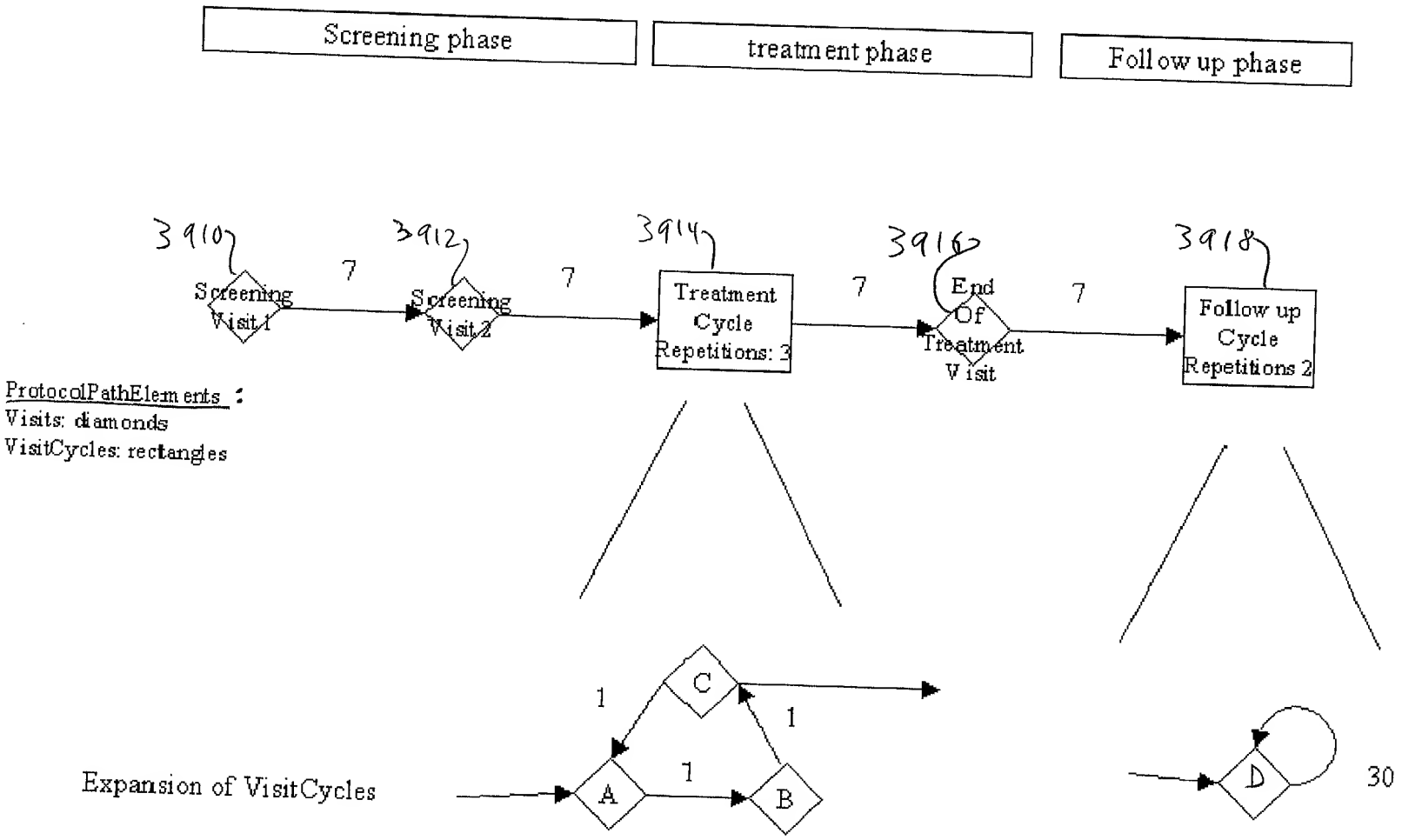
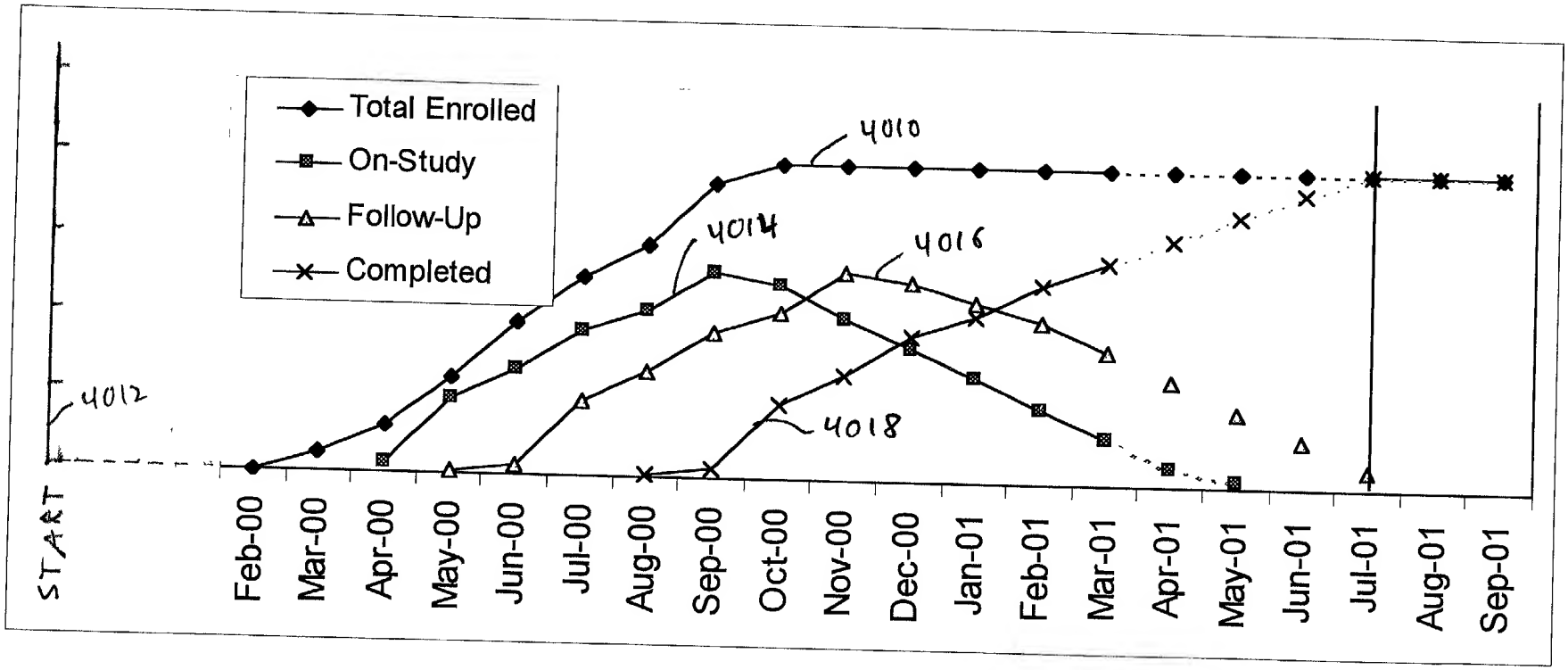


Fig. 39

Forecast Trial Completion



The last patient should complete followup in July 2001

Fig. 40